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CLINIC OF DR. HENRY A. CHRISTIAN

PETER BENT BRIGHAM HOSPITAL

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## LATE APPEARING CLUBBED FINGERS WITH CONGENITAL HEART DEFECTS<sup>1</sup>

GENTLEMEN: Very often one encounters murmurs in examining patients with evident cardiac disease which in quality, position, and transmission differ sufficiently from the murmurs regularly accompanying the usual acquired valve lesions as to arouse a suspicion that they originate in some congenital defect of the heart. If the patient is an adult, has had rheumatism, and presents signs typical of mitral stenosis or aortic insufficiency in addition to the unusual type of murmur, the uncertainty of explanation of all of the physical signs is enhanced. One feels justified in diagnosing, let us say, mitral stenosis, if in the apex region there is heard a late diastolic murmur of rumbling quality and a presystolic thrill is felt, but how to explain the other, unusual type of murmur remains a problem.

Under these circumstances one naturally makes careful inquiry and examination for any additional evidence that will throw light on the diagnosis. With unusual murmurs one thinks of congenital defects or other congenital lesions in the heart, and asks after a history of prolonged cyanosis or having been a blue baby, or seeks for clubbed fingers, which, in the absence of acquired pulmonary lesions, become of so great diagnostic value for a congenital cardiac defect.

<sup>1</sup> From the Medical Clinic of the Peter Bent Brigham Hospital, Boston, Mass.

Even without a history of cyanosis other than would go with the acquired valve lesion and which has only developed when there were numerous other symptoms and signs of cardiac decompensation, the presence of clubbed fingers is a very suggestive evidence of congenital heart lesion, provided there are no physical signs or *x-ray* evidence of chronic pulmonary lesion to cause the clubbed fingers.

It is to be recognized that clubbed fingers do occur without either a chronic pulmonary lesion or congenital heart defect, but they are rare enough under these other circumstances for their presence in any patient who has a heart murmur and no chronic pulmonary lesion to be highly indicative of a congenital heart defect.

In this connection distinction must be made between true and pseudoclubbed fingers. Some people have fingers whose terminal phalanges are widened by reason of the shape of the bone, there being an unusual degree of mushrooming out of the tip of the bone as the bones have developed. Very often those who habitually bite their finger-nails have fingers that have a superficial resemblance to clubbed fingers. Occasionally trauma of the fingers gives a superficial resemblance to clubbed fingers. The true clubbed finger, however, has most change in the soft parts, with some periosteal thickening, but relatively little proliferation of the bone itself, as shown by *x-ray*. The tissues under the base of the finger-nail in true clubbed fingers are soft and give a characteristic spongy feel and rocking to the finger-nail on pressure at its base which is very helpful in diagnosis, and usually there is some cyanosis of the finger-tips unless the patient has a considerable degree of anemia. With rare exceptions there is no difficulty in saying that a given patient has true clubbed fingers.

The exact cause of clubbed fingers is not understood. The explanation that best fits with their occurrence is that they result from anoxemia rather than from simple cyanosis. Their late appearance in some patients in association with progressing acquired valve lesions is in accord with this explanation. This latter type, namely, the clubbed fingers developing fairly late,

often in adult life, in association with acquired valve lesions, I think has not been sufficiently stressed. Their diagnostic significance is very well illustrated by the patient that I will now present.

O. H., female, aged twenty-six, P. B. B. H., Med. No. 20,052, was first admitted to the Peter Bent Brigham Hospital on December 12, 1922 and discharged on December 23, 1922. She was readmitted on March 21, 1923 and died on April 3, 1923. She was a young married woman, had been married seven years, but had had no pregnancies or miscarriages. At the age of ten she had acute tonsillitis followed shortly thereafter by acute rheumatic fever. At this time she was admitted to the Children's Hospital in Boston, having been admitted June 20, 1906, with a temperature of 103° F. At that time her heart was enlarged, the right border of dulness being 4 cm. and the left border of dulness 13 cm. from the midsternal line. There was a marked systolic thrill at the apex and a prolonged high-pitched systolic murmur. There was a short diastolic murmur along the left sternal margin. The liver was enlarged and tender. The elbows and wrists were swollen and tender. The pulse was described as collapsing. Two weeks after admission, dulness, bronchial breathing, and increased whispered voice sounds were noted over the base of the left lung behind, but these signs were absent at the apex and at the extreme base of the lungs. No mention was made of cyanosis or clubbed fingers in her physical examination at the Children's Hospital. She was discharged with a diagnosis of acute rheumatic fever, mitral stenosis and regurgitation, lobar pneumonia. She continued to have frequent attacks of tonsillitis and rheumatic fever from this first attack up to two years ago, at which time her tonsils were removed, and since then she has had no attacks of either. From time to time she has had evidence of decompensation and has taken digitalis. Early in October, 1922 she noticed increasing shortness of breath and that her abdomen was enlarging. At this time her legs began to swell, especially around the ankles. For about a month and a half she had been confined to bed.

On admission to the Peter Bent Brigham Hospital for the first time she was cyanotic and orthopneic and slight exertion produced dyspnea. The fingers were definitely clubbed. There were edema of the dependent parts, ascites and an enlarged liver, a few crackles at the bases of the lungs behind, and a diffuse cardiac impulse, with a very large heart, the right border being 4.2 cm. and the left border 19 cm. from the midsternal line. In the apex region a systolic thrill was felt. Along the left border of the sternum a diastolic thrill was felt as well as a systolic. All over the precordium systolic and diastolic murmurs were present, practically replacing the heart sounds. Both murmurs were much louder and rougher in the pulmonic area than in the apex region. The radial pulse was rather small in volume. Blood-pressure was systolic 120 mm. of mercury, diastolic 90. At this time Dr. Frothingham made a presumptive diagnosis of mitral stenosis and regurgitation, with pulmonic stenosis and regurgitation. A day or two later, noting a continuous thrill all over the precordium but less marked in the aortic region than elsewhere, with the definite clubbing of the fingers and marked cyanosis, I made a presumptive diagnosis of a congenital lesion, either a septum defect or patent ductus arteriosus, in addition to a mitral stenosis and insufficiency. An x-ray taken at about this time showed a definite prominence in the silhouette in the region of the left auricle, and a second prominence higher up in the region of the pulmonary artery, with marked enlargement of the heart to both the right and left. There also were seen areas of increased density in the region of the auriculoventricular septum, suggesting to Dr. Sosman, our roentgenologist, the presence of calcification. Electrocardiograms at this time showed auricular flutter. A sample of arterial blood was found to have an oxygen content of 19.67 per cent. and an oxygen capacity of 22.24 volumes per cent. This was interpreted by Dr. Grant as a saturation only very slightly below the value often found in decompensated cardiac patients.

Discussing the case on staff rounds a day or two later I made the following note: "I think there can be no doubt that

with the tonsillitis and acute rheumatic fever in the past the patient acquired a cardiac lesion. The clubbed fingers have been of particular interest because, although common in congenital cardiac and acquired pulmonary disease, they are rare in acquired heart disease. The character of the thrill which is so marked and occupies both systole and diastole is also of interest. There is a possibility that the patient had a congenital heart lesion which did not show itself until she acquired an additional lesion with the rheumatic fever. In addition to the congenital lesion it seems most probable to me that she has a buttonhole mitral valve and relative tricuspid insufficiency leading to the large liver and cyanosis, but the heart muscle is good enough to keep her fairly comfortable. Electrocardiograms show auricular flutter and heart-block and she is probably on the road to auricular fibrillation." At this time the patient's physician said he had noted the clubbed fingers two years ago, but was sure that they were not present six years ago.

A few days later her vital capacity was found to be 75 per cent. of normal. She was discharged with the diagnosis of mitral stenosis, tricuspid insufficiency (?), pulmonary stenosis (?), congenital cardiac lesion, septum defect or patent ductus arteriosus chronic pericarditis (?), auricular flutter, and clubbed fingers. Physical examination and x-ray had given no evidence of chronic pulmonary lesion.

At home she became gradually more dyspneic and orthopneic, her abdomen continued to swell and the edema increased, so that she returned to the hospital on March 21st. The day following admission I made the following note:

"At the apex, which is out in the midaxilla, there is a vibratory systolic thrill of marked intensity. There is a slight diastolic thrill over the rest of the precordium, while in the pulmonic area there is a systolic thrill and, in addition, a marked vibratory diastolic thrill. Corresponding to these thrills there are harsh murmurs, and both the systolic and diastolic murmurs are well transmitted from the pulmonic area out to the shoulder region. The patient has marked ascites."

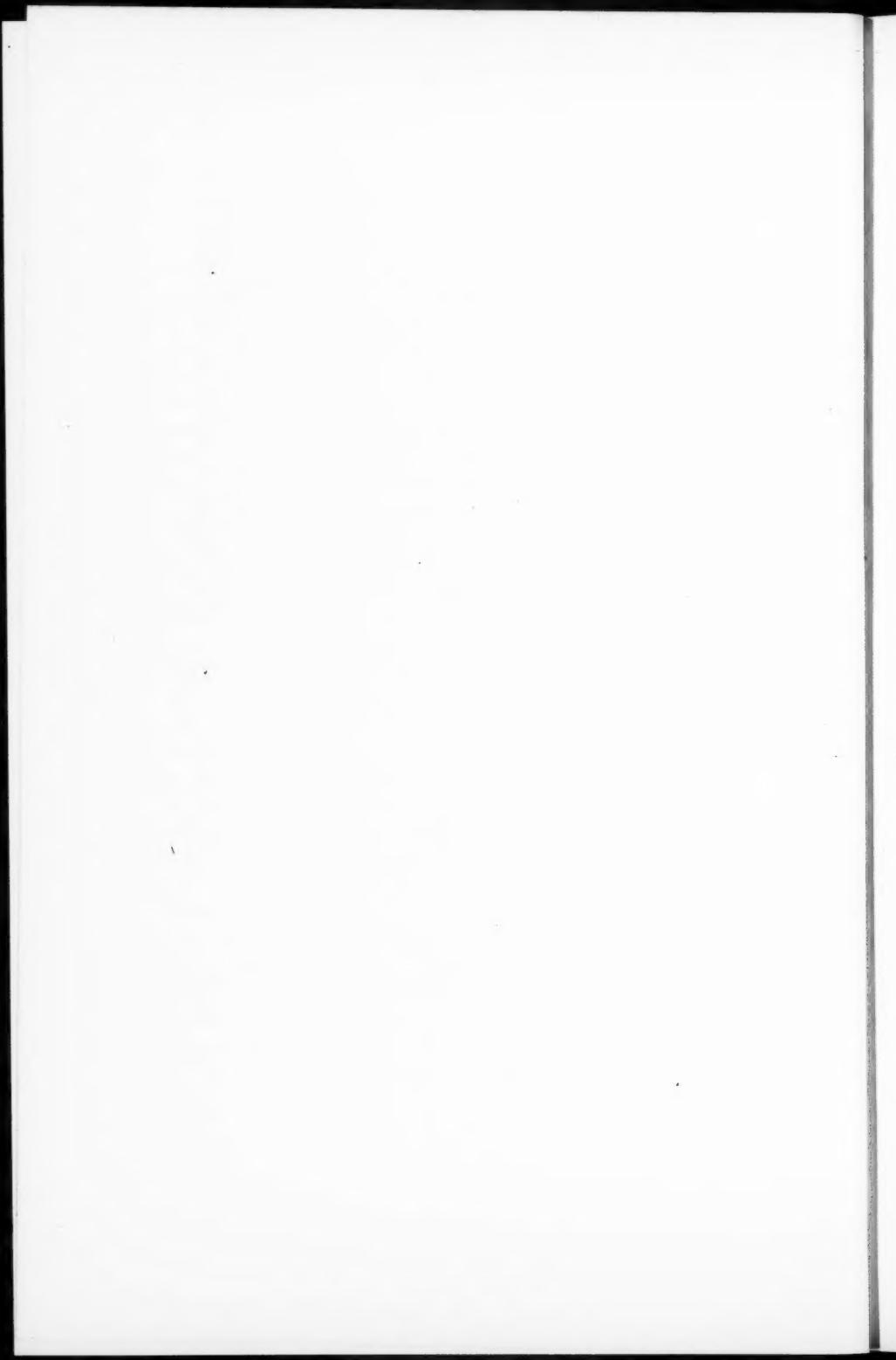
Dr. Frothingham, in examining the patient, added to his

previous diagnosis, adherent pericardium. The patient instead of improving, progressed, and died on April 3d. Autopsy showed congenital heart disease with an interventricular septum defect, anomaly of the tricuspid valve, mitral stenosis, pulmonary stenosis, slight tricuspid stenosis, adherent pericardium, fibrous mediastinitis, calcification in the valves and pericardium. The aortic valve was perfectly normal. The mitral valve was stenosed, calcified, and rigid. There was calcification in the papillary muscles on the left. The tricuspid valve was thickened on the internal leaflet, and this leaflet had a definite anomaly, in that the chordæ tendineæ passed through the defect in the septum and were attached to the papillary muscles in the left ventricle. The pulmonary valve was markedly stenosed and calcified. Below the stenosed pulmonary valve there was another annular area of calcification and the papillary muscles of the right ventricle also showed some calcification. The heart weighed 1020 grams.

The interesting features of this case center around the combination of congenital and acquired cardiac lesions. The history gave the usual etiologic causes of acquired cardiac lesions. The physical examination gave evidences of valve lesions. All who saw the patient interpreted these as indicating mitral stenosis, and one added the opinion that the patient also had pulmonic stenosis, and another, that there was tricuspid insufficiency. It was not thought that there was an aortic lesion. On the basis of *x-ray* examination it was thought there was definite evidence of chronic pericarditis, though there was no positive evidence on physical examination of this condition. The findings at the Children's Hospital sixteen years ago were of interest in this connection, for they suggest the compression signs in the lower left base of acute pericarditis, Ewart's sign, rather than lobar pneumonia, as was diagnosed. Mitral stenosis was recognized at this time.

The unusual murmur in the pulmonic area and the clubbed fingers gave the clue to the existing congenital defect of the heart, and this clinical diagnosis was confirmed at autopsy. The late development of the clubbed fingers is of much interest.

Why did they not appear earlier? They were not noted when she was in the Children's Hospital in 1906, and her family physician, who noted them in 1920, feels sure that they were not present in 1916. Could it be that the development of the pulmonic stenosis caused a change in the circulatory relations that led gradually to the establishment of the cause of clubbed fingers? This seems a definite possibility. Perhaps the acquired pulmonic stenosis and other valve lesions caused an admixture of blood from the two sides of the circulation which had not been present when the septum defect alone existed, and so caused the clubbed fingers. Perhaps in this way anoxemia developed late in this case, and so clubbed fingers appeared late. The clubbed fingers cannot be more definitely explained until we know more of the mechanism of their cause than we do at present. However they are produced, they have a very definite diagnostic value, and in cardiac cases, such as this, justify a diagnosis of the presence of a congenital cardiac defect among other cardiac lesions.



## CLINIC OF DR. ELLIOTT P. JOSLIN

NEW ENGLAND DEACONESS HOSPITAL

### DIABETIC COMA AND ITS TREATMENT<sup>1</sup>

DIABETIC coma needless! Von Noorden criticizes this statement, expressed in last year's Shattuck lecture, but the more I reflect upon it the more I believe in it, and I recommend that you investigate each case you see and decide for yourselves its truth or falsity. It is a melancholy fact that in the last ten weeks I have seen 3 cases of coma, of whom 2 have come from the hands of chiropractors and one from a Christian Scientist. The average duration of the diabetes of these 3 cases from onset to coma was 2.7 years, but the average duration of 231 fatal cases of diabetes of similar age periods in my series, treated before the discovery of insulin, was 4.7 years.

TABLE 1  
THE DURATION OF LIFE IN NEEDLESS DIABETIC COMA AND IN DIABETES

Diabetic coma.			Diabetes.		
Case No.	Age at onset, years.	Duration diabetes to coma, years.	Decade.	Total cases.	Duration diabetes to death, years.
3240	15	0.7	10-19	69	3.3
2317	39	2.5	20-39	162	5.3
3382	25	3.0			
Average duration.....	2.7		Average duration.....	4.7	

The origin of all cases of coma cannot be blamed on irregular practitioners. Far be it from me to claim that. It is very easy

<sup>1</sup> In this clinic I have utilized in part material from the third edition of my book, "The Treatment of Diabetes Mellitus," which is being published by Lea & Febiger.

to throw stones, but it is wiser to carry them in one's pocket as a reminder of personal failures in treatment, which a search of memory and of case records will only too surely disclose. When the diabetic diet is discarded, when appetite is allowed to run wild and the ketogenic anti-ketogenic ratio is broken, or, in plain words, the patient eats too much fat and protein for the carbohydrate he can utilize, it is no matter whether with or without the approval of chiropractor or scientist, doctor or friend, that patient is doomed to death in coma.

An intercurrent infection may sometimes be an exception to the rule that coma is needless, but in most cases I would not yield even this. To be sure, an infection brings coma near, and Peters, at Yale, has shown that most comas are precipitated by infections, because in an infection the subject is over-eating not necessarily of food fat and food protein, but just as harmfully of body fat and body protein. If we prevent increased metabolism by sparing the metabolism of body protein or alter the character of the increased metabolism, coma even under such circumstances may be averted. In fact, it will be averted, is my belief. A diabetic Italian at the Boston City Hospital about the year 1905 went through typhoid fever without a suggestion of acidosis, living upon oatmeal and olive oil—nothing else. Newburgh and Marsh and Petré could not have asked for a diet better attuned to their theories. Its counterpart is certainly worth trying with the next infection in a diabetic.

If the infection is general and there is an unequivocal septicemia, the game is up, and there is no reason why euthanasia should not be secured with  $\beta$ -oxybutyric acid and morphin as well as with morphin alone.

The prevention of coma should be taught to all your diabetic patients. If sick from any cause, tell them (1) to go to bed, (2) to drink a glass of hot liquid every hour, (3) to limit food to orange juice or water oatmeal gruel, (4) to take an enema, (5) to keep warm, and (6) in the meantime to call you or some other doctor. No matter if recovery has taken place by the time of your or his arrival, a patient can recover a good many times, but die but once.

What is there left for the doctor to do? This is the oft-repeated query of doctors as well as patients at the diabetic school. The doctor has much to do. Every scrap of medical knowledge he has ever acquired, every atom of medical skill he may possess is needed. In addition to the continuation of such parts of the above treatment as appear indicated (1) he confirms or disapproves the diagnosis, since the supposed diabetic coma may be meningitis, apoplexy, uremia, or due to morphin or what not, (2) if it is an "honest to goodness" coma, as Root telephoned when Case No. 3382 entered, he gives insulin instantly, intravenously and subcutaneously, (3) he protects the heart with hypodermic injections of digitalis and caffein, (4) he gives salt solution subcutaneously and thus protects stomach and kidneys and helps the circulation, (5) perhaps he washes out the stomach, and (6) continues the treatment of the disease, diabetes, and not the symptom, coma. In other words, he does not (a) add fuel to the fire by giving enormous doses of glucose or (b) fan the flame with soda.

Let me enlarge on these two tenets—glucose and alkalis.

(a) If the blood-sugar is over 0.50 per cent., is that not high enough? There must be sugar enough in the body to be burned if you but give enough insulin to burn it. Such a percentage of sugar implies at least 15 to 25 grams of free glucose, and there are also quantities of glucose to draw upon in the form of protein, which is equivalent to 58 per cent. carbohydrate, setting aside other possible sources of carbohydrate stored as glycogen, which autopsies of such cases disclose. The patient will not burn over 100 or 150 calories an hour, and if you can force him to burn even 20 to 40 of these calories in the form of carbohydrate, he is saved! 'Tis said, give glucose in coma to protect the insulin! I say, to give glucose to a patient in coma to protect the insulin when the blood-sugar is high or the freshly passed urine contains sugar, so long as blood-sugar tests can be performed or a catheter kept in the bladder, shows lack of appreciation of the fundamentals of diabetic treatment, namely, to reduce the blood-sugar and the glycosuria. Give your insulin to protect the patient and not glucose to protect the insulin.

(b) And as for alkalis, why give them? Look at Table 2. Here are 15 recoveries from near coma without alkalis. Before you students as doctors ever give alkalis to your patients with coma, I advise you to look for another list of 15 diabetics as nearly in coma as these who were also treated successfully with alkalis. Dr. Geyelin has at least 2 cases with recovery with CO<sub>2</sub> values at the lower limits of the table, and I am confident that I could lower its upper limits if I drew on the experience of Newburgh and Marsh and Bertrand Smith, who treat acidosis without alkalis. The alkalists, driven from the administration of large doses of alkalis, now recommend doses not to exceed 1 or 2 tablespoonfuls a day, and the very elect of the alkalists acknowledge that about 4 out of 5 cases need no alkalis at all! Do you think there is any case of diabetes whose tissues are so robbed of sodium, potassium, calcium, and magnesium and whose kidneys are so devoid of the power to form ammonia that 1 ounce of soda will save him? A diabetic in coma, who recovers while taking alkalis, in my opinion recovers in spite of alkalis and not because of them.

Coma is a medical emergency. After successful operation in a surgical emergency the nurse wipes the surgeon's brow, gives him a lunch, and the hospital furnishes him the best private room for the rest of the night. Not so with diabetic coma. Doctor and nurse must be on the job day and night, every hour in the twenty-four, either at the bedside of the patient or in the laboratory of the hospital or improvised laboratory of the home for one, two, or three days. This is an acute complication which makes the physician feel he is on a par with the surgeon, so far as saving life is concerned, and the same importance should be attached to the services of each.

This article is not written thoughtlessly. It is the culmination of a survey of the results of treatment of about 1000 cases with alkalis and 2000 without. Perhaps I am wrong. If so, it will be proved, and the sooner the better, so that methods may be changed, but to bring conviction Table 2 must be bettered and the 2 cases Dr. Root will show you, the one treated with and the other without insulin and both without alkalis, must be

TABLE 2  
RECOVERY FROM IMPENDING COMA WITHOUT ALKALI OR INSULIN

Case No.	Date.	FeCl <sub>3</sub>	NH <sub>3</sub> gm. (24- hour amt.)	Plasma CO <sub>2</sub> combining power, vols. per cent.	Alveolar CO <sub>2</sub> mm. Hg. tension.	Notes.
755	Apr. 15, 1917	+	1.6	....	18	
786	June 11, 1916	++	3.9	....	18	
938	Nov. 2, 1917	++++	1.3	....	18	
942	July 13, 1916	++	...	3.7	17	
1011	Sept. 25, 1917	++++	4.3	....	15, 15, 16	
	Sept. 26, 1917	++	...	....	18	
1012	Sept. 13, 1917	+++	...	....	14, 15	Deep respiration.
	Sept. 14, 1917	++	2.5	30	16	
1120	Sept. 7, 1916	+	...	....	18	Deep breathing.
1196	Dec. 10, 1916	+++	3.3	....	18	Nausea, vomiting, air-hunger. Nausea.
1200	May 29, 1917	+++	2.3	....	18, 18	
1410	Oct. 21, 1917	++++	...	....	16, 16	
	Oct. 22, 1917	++	...	....	16, 17, 16	Air-hunger, vomiting.
1566	June 30, 1919	+++	...	18	12	
	July 1, 1919	++++	3.4	....	15	
	July 2, 1919	++	3.2	33	21	
1673	Sept. 7, 1920	++	3.1	26	18	
	Sept. 24, 1920	+	3.05	....	18	
	Sept. 30, 1920	+	5.5	....	14	
	Oct. 4, 1920	+	...	27	....	
	Oct. 5, 1920	+	7.2	....	....	
	Oct. 9, 1920	+	...	....	16	
2074	Nov. 16, 1921	+++	...	23	18	Air-hunger.
2218	June 13, 1922	++++	...	....	18	Air-hunger.
2366	Sept. 29, 1921	++++	3.0	15.9	14, 11	Soft eyeballs, vomiting. Kussmaul respiration, stuporous, but could be roused.
	Sept. 30, 1921	+++	4.4	....	22, 22, 22	
	Oct. 1, 1921	++	...	....	26, 28	
	Oct. 3, 1921	+	3.8	33	32, 30	

surpassed and other physicians in the country must treat a coma case as successfully as Dr. Shedd, whose patient came back to life with insulin, trifling glucose, and 3 grams of sodium bicarbonate.

#### DIABETIC CLINIC AT NEW ENGLAND DEACONESS HOSPITAL

DR. HOWARD F. ROOT

#### TWO CASES OF DIABETIC COMA

Recovery from diabetic coma when the eyeballs have been soft and the CO<sub>2</sub>-combining power of the plasma has been below 16 volumes per cent., though not so rare as formerly, is of sufficient interest to justify discussion of 2 cases, one treated with and one without insulin, but both without alkalis.

Case I: Joslin, No. 2366. Elmer P., age fifteen years, entered the New England Deaconess Hospital in the evening of September 27, 1921, with 3.5 per cent. of sugar in the urine and a + + + ferric chlorid reaction. He had had diabetes for eleven months, during which time he had lost 15 pounds from his maximum weight, and then weighed 74 pounds. Three months previously he had had transient blindness for one day and had been obliged to give up school on account of increasing weakness. Diacetic acid had been found in his urine two days before admission and he had been taking fat and protein in excess of his diet in the form of muffins made from non-carbohydrate flour. During the preceding twenty-four hours he had complained of nausea and pains in the stomach. He was pale, wan, and drowsy and the tension of the CO<sub>2</sub> in the alveolar air was 25 mm. Hg. During the night he was given 1700 c.c. of warm fluid containing 38 gm. of carbohydrate and no fat. The next day he had increasing pain in his stomach, nausea, and vomiting. Table 3 gives results of analyses of blood and urine.

During the first two days gastric lavage was performed twice. On account of vomiting the oral administration of liquids was discontinued and an attempt to give saline and glucose solution by rectum, vein, and subcutaneously was made. He soon ceased to retain rectal fluids and, accordingly, he received saline solution 400 c.c. at a time thrice on September 29th. He was so thin that subcutaneous administration in sufficient quantities was practically impossible. On September 29th his eyeballs were extremely soft, respiration was typically Kussmaul in type, and he could barely be roused. On September 30th he did not vomit, and from this time on he slowly gained strength so that he was discharged on November 7th acid free, but not sugar free, on a diet of carbohydrate 6 grams, protein 15 grams, and fat 33 grams. From that time on he followed dietary instructions faithfully, with the result that in spite of such complications as an acute otitis media in January and ascites which required paracentesis in March, 1922, he has taken insulin since December 19, 1922 and has gained 15 pounds. When

TABLE 3. CASE No. 2366  
RECOVERY FROM ACIDOSIS WITHOUT INSULIN OR ALKALIS

Date, 1921.	Urine:	Sugar, grams.	FeCl <sub>3</sub> .	$\beta$ -oxybutyric acid, gm.	Plasma CO <sub>2</sub> vols. per cent. saturated.	Blood-sugar, per cent.	N.P.N. mg. per 100 c.c.	Alveolar air CO <sub>2</sub> mm. Hg.	Clinical condition.
September 27 " 27-28 " 28-29	4.8 <sup>1</sup> 3.5	74 98	++++ +++	..... 18.3	27.5	0.36	.....	25	Weak, nauseated, drowsy.
" 29-30	2.8	93	+++	11.8	15.9	0.32	42.0	21	Drowsy, Kussmaul respiration, eyeballs soft, vomiting.
" 30-1 October 1-2 " 2-3 " 4-5 " 24-25	2.0 1.7 2.7 2.0 0.5	61 127 64 3 9	++ ++ + ++ 0	16.5 17.3 16.3 12.5 .....	..... ..... ..... ..... .....	45.0 0.28 0.28 0.28	14 11 11 36	14 22 22 26	Vomited twice, eyeballs soft, can just be roused. No vomiting.

<sup>1</sup> Admission specimen.

seen on August 20, 1923 he looked well, and since then has returned to school on a diet containing 1749 calories.

Case II: Joslin, No. 3382. Mrs. F., aged twenty-eight years, entered the New England Deaconess Hospital September 15, 1923, at noon, having had labored respiration for six days and complete coma for four hours. She had had diabetes for three years, but had broken diet liberally during the last three months. She had typical Kussmaul respiration, the pulse-rate was 132, hands and feet cold, and the rectal temperature was 95° C. The plasma CO<sub>2</sub>-combining power was 10.9 volumes per cent. The blood-sugar was 0.54 per cent. and the non-protein nitrogen 65.6 mg. per 100 c.c. The eyeballs were so soft that Dr. L. P. Tingley was unable to measure the tension with a tonometer; 1800 c.c. urine, obtained by catheter, contained 1.8 per cent. sugar and gave a ++++ ferric chlorid test.

The patient was immediately given 20 units of insulin by vein and 20 units subcutaneously, a subpectoral injection of 1200 c.c. saline, and an enema of 1 quart saline, which she retained. Mindful of the danger of a dilated stomach, fluids were given by mouth at the rate of 50 to 100 c.c. per hour only; 10 grams levulose in black coffee and 100 c.c. orange juice were taken during the late afternoon, but in spite of these precautions vomiting occurred and gastric lavage was performed at 11 P. M.; 30 grams carbohydrate as rectal glucose was also given, but was not retained. Digitalis and caffeine were administered alternately every four hours for the first thirty-six hours.

Table 4 gives analyses of the blood and urine with the insulin dosage during the first twenty-one hours.

At the end of twenty-one hours the patient had received 220 units of insulin, and (1) the urine was sugar and acid free, (2) the blood-sugar was 0.17 per cent., (3) the plasma CO<sub>2</sub>-combining power was 71 volumes per cent., (4) though very drowsy and weak, she was conscious and rational, and (5) the eyeballs were of nearly normal tension.

On September 26th she was receiving 50 units of insulin, the urine was free from diacetic acid, though containing 0.3 per cent. sugar, and the blood-sugar was 0.30 per cent. The

TABLE 4. CASE No. 3382

Date, 1923.	Urine:		Blood:			Insulin units.
	Sugar, per cent.	Diacetic acid.	Sugar, per cent.	CO <sub>2</sub> vols. per cent.	N. P. N. mg. per 100 c.c.	
Sept. 15 Adm.	1.8	++++	0.55	10.9	65.6	40
2 hours	0.7	+++	0.56	29.0	44.8	20
4 "	0.6	++	...	...	...	20
6 "	0.5	0	0.50	29.6	49.2	20
8 "	0.5	0	0.59	20.8	29.0	
10 "	0.3	0	...	...	...	
12 "	...	...	...	...	...	30
14 "	...	...	...	...	...	20
16 "	...	...	...	...	...	20
21 "	0	0	0.17	71.2	36.0	20
Total	...	...	...	...	...	220

diet consisted of carbohydrate 48 grams, protein 46 grams, and fat 119 grams. Intraocular tension had returned to normal and recovery was assured, and (October 10th) has taken place.

In uncomplicated diabetic coma excessive treatment may be as harmful as half-way measures. Caution in the giving of fluids by mouth is of first importance. It is possible to produce dilation of the stomach, cardiac embarrassment, and failure by forcing fluids through a stomach- or duodenal tube. In most cases 50 to 100 c.c. of fluid per hour by mouth are sufficient, provided saline solution is given subcutaneously, rectally, or intravenously up to 2000 c.c. in twenty-four hours.

The effect of insulin is not entirely measurable in terms of the blood-sugar. Case 2 began to show signs of returning consciousness within three hours after the first dose of 40 units, yet her blood-sugar was not lowered at the end of eight hours, when 100 units had been given. An initial dose of 40 units is, in general, a reasonable amount in coma. Thereafter doses of 20 units every two or three hours may be given safely if the urine contains sugar or diacetic acid. Large amounts of glucose as a buffer against the insulin are rarely necessary.

## PRACTICE OF DR. GEORGE H. SHEDD

NORTH CONWAY, N. H.

## RECOVERY FROM DIABETIC COMA WITH INSULIN

**Introduction.**—E. P. Joslin: The following case of recovery from diabetic coma will show that diabetic coma can be treated successfully by the general practitioner, and I have persuaded Dr. Shedd to allow its report in the Medical Clinics of North America. Far better medicine is carried on in small towns than many realize or admit. Common sense counts. This Case, No. 2801, which was one of the severest to have come under my care, recovered from actual coma through the unaided efforts of Dr. Shedd. He gave insulin until he obtained results. The total quantity of sodium bicarbonate administered the patient amounted to 3 grams during the two days, and this by enema. The total amount of carbohydrate given the patient during these two days consisted of the juice of two oranges by mouth and 30 grams of glucose by enema.

C. S., aged fifteen, developed symptoms of diabetes acutely in June, 1922, and the disease was diagnosed July 26th. She was sent to the New England Deaconess Hospital July 28, 1922, where she remained, or at Mrs. Leatherbee's diabetic boarding house, the greater part of the time until May, 1923. After a few weeks at home she made a trip to New York. From onset the case was considered severe, and even with 35 units of insulin she had difficulty in remaining sugar free. Her unusually large adolescent goiter was left alone by the advice of all consultants. Unfortunately on various occasions she broke her diet.

Upon June 8th the patient developed nausea and abdominal pain; upon June 9th difficult breathing with vomiting and continued nausea and pain, together with delirium; and on June 10th these symptoms persisted, and between 3 and 5 A. M. she was unconscious, with deep respiration.

The patient received water freely by mouth during June 9th and 10th, save when delirious, but the only food consisted of the juice of two oranges. On June 9th she was given three

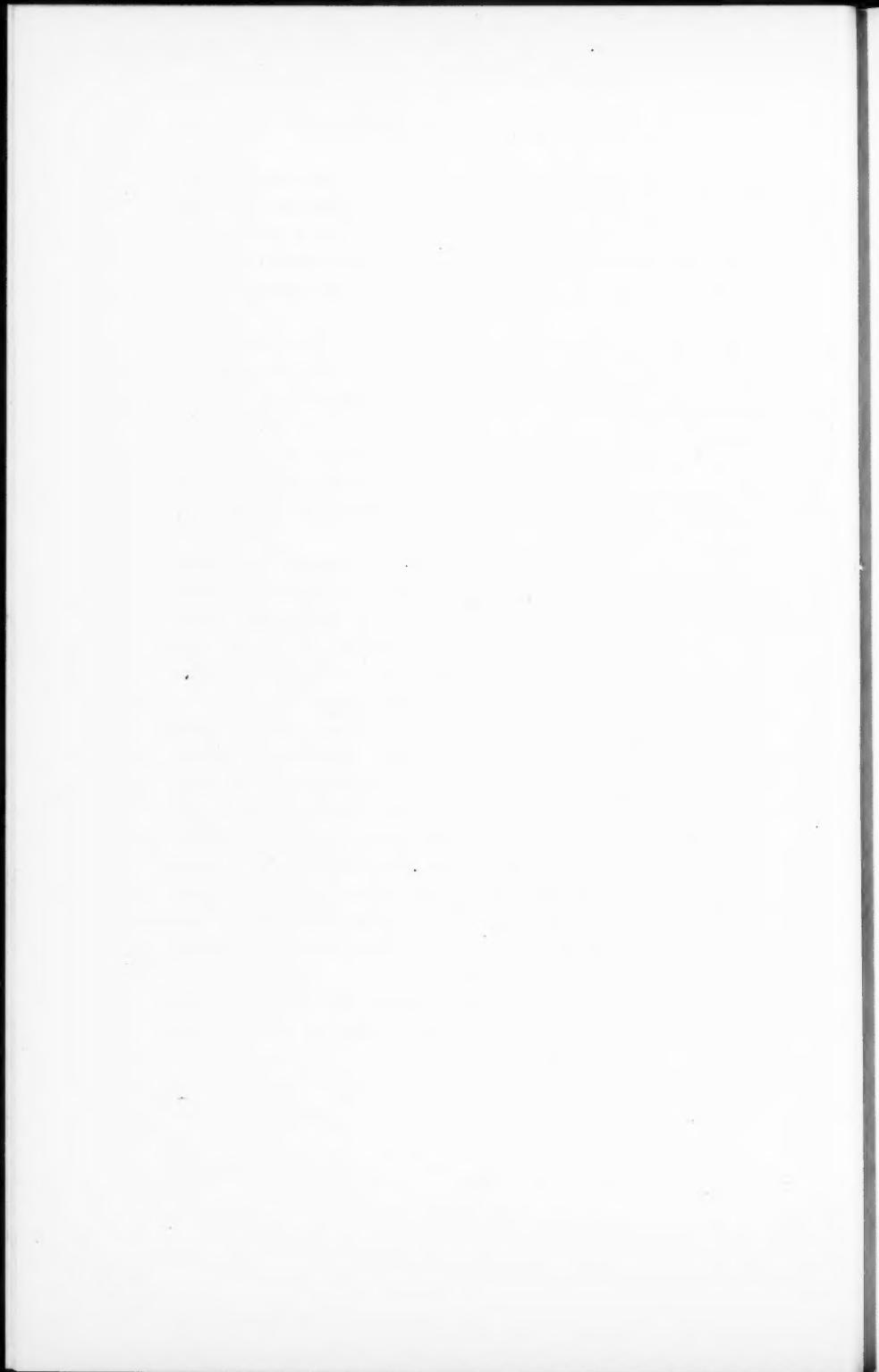
enemata. The first consisted of 4 ounces of 10 per cent. glucose solution made up in 1 per cent. sodium bicarbonate, and this was retained for one-half hour. Later in the day 3 ounces of a similar solution were given, which were retained for two hours, and still later the same quantity, which was retained for three hours.

Upon the morning of June 9th 10 minims of adrenalin chlorid were given coincidently with insulin. The insulin was given as follows: June 9th, 180 units; June 10th, 240 units in 60-unit doses at 6 A. M., 9 A. M., 11 A. M., and 3 P. M.

The breathing became easy at about 3 to 4 P. M. on June 10th, and the pulse, which was 140 in the early morning, fell to 120 at noon and later to 96. The patient was then sent to Boston.

When the patient reached the New England Deaconess Hospital on June 10th after a journey of seventy-four miles she was drowsy, had deep respiration, but the eyelids were firm and the pulse 112, the CO<sub>2</sub> in the alveolar air 17, and the CO<sub>2</sub> in the blood 36 volumes per cent. and the blood-sugar 0.33 per cent. The urine contained 3.5 per cent. sugar with +++ diacetic acid and many granular casts, but a specimen obtained one hour later gave but 1 per cent. sugar. On account of the falling blood-sugar but 10-unit doses of insulin were given during the remainder of June 10th up to June 11th at 5 P. M. A recurrence of severe acidosis then took place, with the omission of insulin during the night of June 11th to 12th, as on two earlier occasions, with this same patient. At 8 A. M. on June 12th the CO<sub>2</sub> was 16.5 volumes per cent. and the respiration of the Kussmaul type. With insulin in 10-unit doses four or five times in twenty-four hours she recovered.

Subsequently the patient went home, did not invariably adhere to her diet, and during August contracted a bronchitis, and death in coma ensued.



## CLINIC OF DR. REGINALD FITZ

PETER BENT BRIGHAM HOSPITAL

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### THE TREATMENT OF DIABETES MELLITUS<sup>1</sup>

1. The "Allen" Treatment.
2. The "Joslin" Treatment.
3. The "High Fat" Treatment.
4. Insulin.

THE last few years have seen a rapid growth in research upon diabetes mellitus in this country. New laboratory methods applicable to clinical studies have been devised for observing the chemical and metabolic phenomena of the disease; scientific dietetics have been developed and have come to play a more than ever important part in treatment; varied and diverse types of diets have proved valuable in the treatment of individual cases; and, finally, a voluminous and technical literature upon different phases of the disease and its treatment has grown up. One result of this concentrated interest in diabetes has been, it seems to me, that the general practitioner and medical student are often bewildered by the conflicting opinions which they hear and read in regard to the best methods of handling actual cases. The advent of insulin will throw upon the hospitals and doctors of this country the burden of treating more diabetics than formerly. Since no one believes that the dietetic treatment of diabetes will become less important with the use of insulin, the general practitioner and medical student must be more eager than ever to familiarize themselves with the various accepted types of dietetic procedure which, with or without insulin, are at their disposal for controlling any given case.

<sup>1</sup> From the Medical Clinic of the Peter Bent Brigham Hospital, Boston.

At present nearly all American diabetic clinics are following their cases according to one of three systems: they are using modifications of the "Allen" method of treatment, the "Joslin" method of treatment, or the "high fat" method of treatment. Each of these methods produces results which are usually of immediate benefit to the patient, and at present no one is certain which will prove best in the long run of time. The "Allen" and "Joslin" methods attack the problem of diabetic therapy from an opposite point of view to that held by the advocates of the "high fat" methods; all three programs have conscientious and fair-minded upholders.

I propose today to describe as simply as I can what is meant by the "Allen" treatment, the "Joslin" treatment, and the "high fat" treatment in a case not receiving insulin, and to point out the essential differences between these three procedures by case records. I shall also talk for a few minutes about insulin.

#### THE "ALLEN" TREATMENT

The "Allen" treatment owes its origin to F. M. Allen, of Morristown, New Jersey. The original paper describing it was published in 1915 in the Boston Medical and Surgical Journal, vol. 172, p. 743, under the title of "The Treatment of Diabetes." Allen subsequently modified his original views in certain details, but, on the whole, has maintained a consistent point of view supported scientifically by numerous animal experiments.

In brief, Allen sees in diabetes a weakness of the pancreatic function for the proper assimilation of carbohydrates, proteins, and fats, and defines the best treatment as an attempt to relieve overstrain of this weakened assimilative function by limitation of all components of the diet. Relief is most quickly obtained by fasting or reduction of diet until glycosuria disappears and the blood-sugar concentration becomes nearly normal. When glycosuria is no longer present the diet is gradually built up, the aim being to control from the outset hyperglycemia, acidosis, and all other diabetic manifestations.

The details by which the treatment is carried out vary in each case, but are guided by the following general principles.

The total calories of the diet should be very low at first and should be increased very gradually. Protein is the most important of the food elements. The tolerance for protein is highest when other foods are excluded or closely restricted. The caloric requirement of the individual falls with the body weight, while tolerance rises as weight falls. Eventually a diet should be established which is sufficiently high to maintain the patient at a lower level of weight and metabolism than is his normal, and at a level which is sufficiently low to control hyperglycemia and glycosuria. The diet by which this is accomplished is so balanced as to maintain nitrogen equilibrium and to prevent acidosis, while at the same time it is as high as possible to fulfil the preceding requirements. The end-result by this method often means a considerable reduction of the patient's body weight and strength as compared with the level that can be maintained on higher diets; its justification depends on the belief that diabetic patients are better off in the long run when their weakened functions are spared as much as possible, since in that way the return of symptoms and downward progress is prevented.

The first case record which I shall show is from a case treated at the Rockefeller Hospital according to this plan. I feel justified in discussing this case because I helped to take care of the patient in association with Dr. Allen and Dr. Stillman.

The patient<sup>1</sup> was an American schoolgirl twelve years old who entered the hospital November 16, 1916. There was no family history of diabetes. The patient began to feel ill about a year previously when diabetes was first recognized, and came to the hospital on account of progressive weakness, especially marked during the previous two months. By way of care she had been given a starch-low fat-rich diet.

Physical examination was essentially negative except for emaciation and for evidence of chronic infection of two teeth and about the gums. The details of treatment employed are shown in the table on page 652.

<sup>1</sup>This patient was Case 72 described by Allen, Stillman, and Fitz on page 451 of Monograph 11 of the Rockefeller Institute for Medical Research.

TABLE I

Date, 1916.	Weight, kg.	Diet.			Urine.			Blood.		
		Carbo- hydrate, gm.	Protein, gm.	Fat, gm.	Calories.	Nitrogen, gm.	Sugar, gm.	Total ace- tone bodies, gm.	Sugar, mgn.	Total ace- tone bodies per 100 c.c.
Nov.	31.6					13.6	89.0	23.6	310	41.6
5	31.6					8.2	19.0	14.0		33.8
6	31.6					7.5	13.1	9.8	220	61.5
7	31.6					7.1	10.5	6.5		30.5
8	31.6					7.5	11.7	5.1	250	
9	31.6					7.5	5.9	5.5		48.8
10	31.6					5.9	7.0	10.4		57.0
11	31.6					5.6	6.2	4.7		
12	31.6					5.6	6.2	4.6	280	51.3
13	31.6					5.6	6.2	3.1		46.0
14	31.6					5.5	8.3	2.1		
15	31.6					4.7	2.5	2.8		
16	31.6					4.9	2.9	2.4	230	42.3
17	31.6					4.9	2.9	2.4		55.0
18	31.6					4.2	1.4	1.7		
19	31.6					4.0	Trace.	1.9		
20	31.6					5.9	Trace.	1.2	290	52.2
21	31.6					5.9	Trace.	1.2		60.0
22	31.6					5.6	Trace.	1.0		
23	31.6					5.6	Trace.	2.7		
24	31.6					5.6	Trace.	1.7		
25	31.6					4.4	Trace.	1.6		
26	31.6					3.6	0	1.4		
27	31.6					3.6	0	1.2		
28	31.6					3.6	0	1.3		
29	31.6					3.6	0	1.2	260	36.2
30	31.6					3.6	0	1.2		
31	31.6					3.6	0	1.2		
Dec.	31.6					3.6	0	1.2		
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18	31.6					3.6	0	1.2		
19	31.6					3.6	0	1.2		
20										

As can be seen, the patient proved to be a stubborn case and required a long period of undernutrition before her tolerance began to improve. She was deliberately made to lose weight, so that when she left the hospital she was about 15 per cent. lighter than when she entered. The loss in weight was induced during the thirty-six days she was in the hospital by eleven fast days, seven days when she received less than 100 calories of food, and fourteen days when she received less than 500 calories of food. We have no accurate data on which to judge the number of calories which she required to keep in caloric equilibrium. If we assume, however, that a child of her weight and age would require 30 calories per kilogram, or 780 calories a day, we see that even at discharge she was living on a diet well below her caloric requirements. This diet was maintained to reduce the blood-sugar concentration, which tended to remain persistently elevated, and to clear up acidosis. Had the diet been increased in any way, almost surely, according to Allen's hypothesis, would the blood-sugar concentration have increased and acidosis have developed, thereby speeding up the natural downward progress of the disease.

This case also illustrates the manner in which fasting or very low caloric diets clear up acidosis. The blood-acetone concentration after a slight initial rise fell slowly but surely, and the blood CO<sub>2</sub> was within normal limits on the sixth day and afterward. The excretion of acetone bodies began to diminish as soon as treatment was begun, and quickly became of no significance.

On the whole, this is a fair example of the result of treatment by Allen's method in a very severe case. The points are that by prolonged undernutrition and fasting acidosis and glycosuria were cleared up, ketosis was checked, hyperglycemia was diminished, and the patient was discharged upon a low diet, but one compatible with life. This was accomplished at the expense of considerable body protein, as judged by the nitrogen balance, and by a reduction in weight of about 15 per cent. The patient died in coma a few months later, having felt fairly well in the interim and having led a fairly normal

life. This outcome was probably inevitable in a case of this age and severity not institutionalized for a much longer time and which could not afford special nurses.

My main reason for talking about this case is to call attention to the fact that prolonged undernutrition with loss of weight actually increased tolerance in this case of maximum severity. I have seen other cases treated in the fashion described, and am convinced, as Allen stated, that prolonged undernutrition will eventually produce tolerance in almost all severe cases sufficient to keep the patient alive, although his weight and strength may remain far below normal. The common mistake which many physicians make in their method of using the "Allen" treatment is the failure to realize that in cases of the type described prolonged undernutrition and fasting must be carried out until tolerance increases; if the course of treatment is interrupted before tolerance is gained and if attempts are made during the course of treatment to save strength by allowing the patient to "eat and show a little sugar" from time to time, the actual result is often a patient debilitated from partial starvation with a tolerance actually lowered by what has been attempted. Such a plan is diametrically opposed to the one outlined by Allen.

#### THE "JOSLIN" TREATMENT

Joslin<sup>1</sup> for many years has been attacking the problems of diabetic therapy from both scientific and practical points of view. Following Allen's first publication he at once accepted the principles of undernutrition therein established, soon recognized the danger of too prolonged fasting in certain cases, and finally attempted to devise a systematic method for making diabetic treatment as safe and easy as possible for the usual run of cases observed in the home or hospital.

With these ideas in mind the "Joslin" treatment guards against the dangers of fasting by a preliminary period of dieting. During this interval the patient is prepared for fasting by first

<sup>1</sup>For a short description of the Joslin treatment see Joslin, E. P., A Discussion of the Newer Methods in the Treatment of Diabetes, Southern Med. Jour., 1922, 15, 93-103.

omitting all fat, so that treatment is begun with a diet which contains about one-half to two-thirds of the carbohydrate ordinarily taken in health and a normal amount of protein. Subsequently the protein and carbohydrate is decreased in an orderly fashion until fasting is instituted. Finally, a system of diets is proposed for use as soon as the urine is aglycosuric, by which the tolerance can be established and on the basis of which the final diet can be built up. The plan of these various diets is shown by the cards on pages 656 and 657.

As can be seen, the test diets are designed for the period during which the patient becomes gradually sugar free. On successive days advances can be made from Test Diet 1 to Test Diet 5, and if on the fifth day the patient is not sugar free, fasting can be employed for one or more days.

The maintenance diets are for use as soon as the urine of the patient is free from sugar. If this occurs as a result of Test Diet 5, the patient begins with Maintenance Diet C<sub>1</sub> PF<sub>1</sub>. The actual articles of food representing the carbohydrate in the diet for the first day are given under the heading of Carbohydrate, for convenience described as C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, etc. The articles referred to under protein and fat are under the heading which, for the same reason, is described as PF<sub>1</sub>, PF<sub>2</sub>, PF<sub>3</sub>, etc. Certain cases of diabetes can proceed steadily day by day from C<sub>1</sub> PF<sub>1</sub> to C<sub>12</sub> PF<sub>12</sub> without showing sugar. If sugar does appear in the urine, the diet is dropped back two days in the carbohydrate group until the urine becomes sugar free, and is then advanced in the protein and fat group until sufficient calories are obtained. Thus, if sugar appears on C<sub>7</sub> PF<sub>7</sub>, the diet prescribed would be that included in C<sub>6</sub> PF<sub>7</sub>, and thereafter progression would be made in the PF group until 25 or 30 calories and a gram of protein per kilogram of body weight per twenty-four hours were furnished the patient.

Occasionally the patient becomes sugar free on Test Diet 2, 3, or 4. It is then unnecessary to begin with Maintenance Diet C<sub>1</sub> PF<sub>1</sub>, but instead with a maintenance diet which contains a value for carbohydrate similar to that of the test diet upon which the patient becomes sugar free.

## DIABETIC DIETS

DIET IN GRAMS.		TEST DIETS.										PROTEIN AND FATTY ACIDS.									
		Diet with which sugar free.	Carbohydrate.	Protein.	Fat.	Chlorides.	Carbohydrate.	Protein.	Fat.	Bread.	Potato.	Wheat.	Shredded Wheat.	Bacon.	Butter.	Meat.	Fish.	Shrimps.	Milk.	Name of Diet.	
T. D. 1	189	89	15	1247	300	300	1	240	90	120	60	60	60	90	90	120	180	90	300	1	
T. D. 2	102	58	0	640	300	300	1	120	60	120	60	60	60	90	90	120	90	90	240	3	
T. D. 3	64	33	0	388	300	300	1	120	60	120	60	60	60	90	90	120	90	90	120	4	
T. D. 4	36	27	0	252	300	300	1	120	60	120	60	60	60	90	90	120	90	90	120	5	
T. D. 5	15	5	0	80	300	300	1	120	60	120	60	60	60	90	90	120	90	90	120	5	
MAINTENANCE DIETS.																					
C <sub>1</sub> + PF <sub>1</sub>	10	11	6	138	300	300	1	300	100	300	100	100	100	300	300	300	100	100	300	1	
C <sub>1</sub> + PF <sub>2</sub>	22	13	18	302	300	300	1	300	100	300	100	100	100	300	300	300	100	100	300	2	
C <sub>1</sub> + PF <sub>3</sub>	32	24	24	440	600	600	15	600	200	600	200	200	200	600	600	600	200	200	600	3	
C <sub>1</sub> + PF <sub>4</sub>	42	29	39	635	600	600	1	600	200	600	200	200	200	600	600	600	200	200	600	4	
C <sub>1</sub> + PF <sub>5</sub>	52	32	53	813	600	600	15	600	200	600	200	200	200	600	600	600	200	200	600	5	
C <sub>1</sub> + PF <sub>6</sub>	63	43	65	1009	600	600	30	600	200	600	200	200	200	600	600	600	200	200	600	6	
C <sub>1</sub> + PF <sub>7</sub>	73	51	70	1126	600	600	30	600	200	600	200	200	200	600	600	600	200	200	600	7	
C <sub>1</sub> + PF <sub>8</sub>	83	60	88	1364	600	600	30	600	200	600	200	200	200	600	600	600	200	200	600	8	
C <sub>1</sub> + PF <sub>9</sub>	96	63	94	1482	600	600	30	600	200	600	200	200	200	600	600	600	200	200	600	9	
C <sub>10</sub> + PF <sub>10</sub>	107	64	94	1530	600	600	30	600	200	600	200	200	200	600	600	600	200	200	600	10	
C <sub>11</sub> + PF <sub>11</sub>	131	76	99	1719	600	600	30	600	200	600	200	200	200	600	600	600	200	200	600	11	
C <sub>12</sub> + PF <sub>12</sub>	155	80	99	1831	600	600	30	600	200	600	200	200	200	600	600	600	200	200	600	12	
Food.		Weight in grams.										Approximate equivalent.									
Orange.....	300.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	
5 per cent. vegetables.....	300.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	
Skimmed milk.....	480.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	
Fish.....	120.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	
Pasta.....	240.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	
Meat.....	90.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	

Approximate equivalent.  
Food. Weight in grams.  
Orange..... 90.....  
5 per cent. vegetables..... 30.....  
Skimmed milk..... 60.....  
Fish..... 30.....  
Pasta..... 30.....  
Meat..... 30.....  
Approximate equivalent.  
Food. Weight in grams.  
One and one-half large size bread..... 90.....  
Three moderate portions oatmeal, dry weight..... 30.....  
One pint, 16 ounces bacon..... 60.....  
Two small portions bacon..... 30.....  
Four tablespoons butter..... 30.....  
Four crispin portions butter..... 30.....  
Three medium portions butter..... 30.....  
Approximate equivalent.  
Food. Weight in grams.  
One small slices bacon..... 30.....  
One large saucerful bacon..... 60.....  
Four tablespoons bacon..... 30.....  
Three medium portions bacon..... 30.....

## DIABETIC DIETS

WATER, CLEAR BROTHS, COFFEE, TEA, COCOA SHELLS, AND CRACKED COCOA CAN BE TAKEN WITHOUT ALLOWANCE FOR FOOD CONTENT

## FOODS ARRANGED APPROXIMATELY ACCORDING TO CONTENT OF CARBOHYDRATES

1 to 3 per cent.	3 to 5 per cent.*	10 per cent.*	15 per cent.	20 per cent.
Vegetables (fresh or canned).				
Lettuce	Tomatoes	String beans	Green peas	Potatoes
Cucumbers	Brussels sprouts	Pumpkin	Artichokes	Shell beans
Spinach	Water-cress	Turnip	Parsnips	Baked beans
Asparagus	Rhubarb	Kohlrabi	Canned lima beans	Green corn
Rhubarb	Sea kale	Squash		Boiled rice
Endive	Okra	Beets		Boiled macaroni
Marrow	Cauliflower	Carrots		
Sorrel	Egg-plant	Onions		
Sauer-kraut	Cabbage	Green peas, canned		
Beet greens	Radishes			
Dandelion greens	Leeks			
Swiss chard	String beans, canned	Watermelons	Raspberries	Plums
Celery	Broccoli	Strawberries	Currants	Bananas
Mushrooms	Artichokes, canned	Lemons	Apricots	Prunes
Fruits.	Ripe olives (20 per cent. fat)	Cranberries	Pears	
	Grape-fruit	Peaches	Apples	
		Pineapple	Huckleberries	
		Blackberries	Blueberries	
		Gooseberries	Cherries	
		Oranges		

\* Reckon average carbohydrate in 5 per cent. vegetable as 3 per cent.—of 10 per cent. vegetable as 6 per cent.

1 gm. protein = 4 calories.  
 1 gm. carbohydrate = 4 calories.  
 1 gm. fat = 9 calories.  
 6.25 gm. protein = 1 gm. nitrogen.

1 kilogram = 2.2 pounds.  
 30 grams (gm.) or cubic centimeters (c.c.) = 1 ounce.  
 A patient "at rest" requires 25 calories per kilogram.

30 grams (1 ounce) Contain approximately	Carbohy- drate, gm.	Protein, gm.	Fat, gm.	Calories.
Oatmeal, dry weight.....	20	5	2	118
Shredded wheat.....	23	3	0	104
Uneeda biscuits, two.....	10	1	1	53
Cream, 40 per cent.....	1	1	12	116
Cream, 20 per cent.....	1	1	6	62
Milk.....	1.5	1	1	19
Brazil nuts.....	2	5	20	208
Oysters, six.....	4	6	1	49
Meat (cooked, lean).....	0	8	5	77
Chicken (cooked).....	0	8	3	59
Bacon.....	0	5	15	155
Cheese.....	0	8	11	131
Egg (one).....	0	6	6	78
Vegetables, 5 per cent. group.....	1	0.5	0	6
Vegetables, 10 per cent. group.....	2	0.5	0	10
Potato.....	6	1	0	28
Bread.....	18	3	0	84
Butter.....	0	0	25	225
Oil.....	0	0	30	270
Fish, cod, haddock (cooked).....	0	6	0	24
Broth.....	0	0.7	0	3

If the protein and fat are too high for the individual on a given day, it is easy to advance the carbohydrate and decrease to an earlier day on protein and fat.

You will notice that the highest diets proposed according to this plan are low in fat. The reason for this is because Joslin thinks that since the ratio of carbohydrate to fat in the normal diet is about 6 to 1, it is reasonable to believe that the nearer the normal ratio of 6 carbohydrate to 1 fat can be preserved with normal blood-sugar concentration, absence of acidosis and glycosuria and without progressive loss of weight, the better it is for the individual. Therefore Joslin purposely keeps the fat content of the diet low for two reasons: to keep the total calories low and the patient in a state of subnutrition, and to keep the diet as normally balanced as is possible under the circumstances.

On the whole, the "Joslin treatment" is very much like the "Allen treatment," in that both are consciously undernutritional cures, but differ in that Joslin avoids fasting as much as he can and is not quite so stringent as is Allen in demanding a constantly normal blood-sugar concentration and low weight. The "Joslin treatment," moreover, is systematic and simple, so that it can be applied in the patient's home. Finally, it aims to afford the patient a low caloric diet balanced as normally as possible in its components of carbohydrate, protein, and fat, preferring to lower the carbohydrate and protein proportions for an increase in fat as a last resort. Both methods make use of occasional fast days or half-fast days as a means of keeping the blood-sugar concentration normal, and both make use of fluids, etc., when indicated.

I shall demonstrate 2 cases treated by the Joslin method, the one with acidosis to compare with the first case, and the other to illustrate how satisfactorily the method works in a mild case.

The first case (P. B. B. H., Medical No. 20,668) is that of an American waiter twenty-two years old who entered the hospital on March 8, 1923. He developed symptoms of diabetes about three years ago, but has not lost greatly in weight or strength despite the fact that he has recently had an acute

TABLE 2

Date. March, 1923.	DIET.				URINE.			BLOOD.			
	Weight, kg.	Carbohy- drate, gm.	Protein, gm.	Fat, gm.	Calories.	Nitrogen, gm.	Sugar, gm.	Total ace- tone bodies, gm.	Sugar, mgm.	Total ace- tone bodies per 100 c.c.	CO <sub>2</sub> vols. per cent.
8.....	66.4	189	89	15	1247	20.0	135.2	23.4			
9.....	66.0	102	58	0	640	18.6	125.0	14.3			
10.....	66.0	64	33	0	388	15.4	118.0	13.2	250	71.5	38.0
11.....	66.0	36	27	0	252	12.6	63.0	15.8			
12.....	66.0	15	5	0	80	9.6	50.0	10.8	210	85.4	46.2
13.....	65.6	Fast day.	..	..	..	7.8	34.0	10.9	190	72.5	48.2
14.....	65.6	Fast day.	..	..	..	5.7	23.9	8.2			

respiratory infection. His family and previous histories are unimportant. His physical examination is negative except for enlarged tonsils, which appear to be infected. During the first seven days of hospitalization he was given the "Joslin treatment." The table on page 659 shows what happened during these seven days.

As can be seen, just as in the case treated by the "Allen method," so in this case, treated by the "Joslin method," there was an immediate fall in the nitrogen, sugar, and acetone bodies excreted, while in the blood the sugar concentration diminished, and acidosis, as measured by the blood CO<sub>2</sub>, rapidly disappeared. One interesting feature was that the blood-acetone bodies increased at first despite the fact that their excretion diminished and that the blood CO<sub>2</sub> rose. I believe this apparent contradiction of the ordinary rules of acidosis depends on the fact that the Joslin test diets are alkaline diets and that the result obtained in regard to this particular detail was very much as if 5 or 10 grams of bicarbonate had been given on an "Allen" fast day. My reason for thinking this is because I have frequently seen the blood-acetone concentration and CO<sub>2</sub> rise in cases treated with soda, while in untreated cases on a mixed diet the blood CO<sub>2</sub> rises as the blood-acetone body concentration falls.

The second case (P. B. B. H., Medical No. 20,263) is that of a man fifty-three years old who entered the hospital January 10, 1923. He knows that he has had diabetes for at least five years. In addition, he now has arteriosclerosis and frequent attacks of angina pectoris. His family and previous histories are unimportant. His physical examination shows him to be 5 feet, 8 inches tall, and to weigh 185 pounds, or, in other words, to be nearly 25 pounds overweight for his age and height. Besides being too fat he also has considerable obvious arteriosclerosis, an enlarged heart, and a systolic blood-pressure of 240. His kidney function is satisfactory. In brief, he represents the common, middle-aged type of diabetic with whom you are all familiar, who owes some of his diabetes to earlier overeating and underexercising, and who must now be treated not only for

TABLE 3

Date. January, 1923.	Weight, kg.	DIET.			Calories.	Diet No.	URINE.		BLOOD.
		Carbohydrate, gm.	Protein, gm.	Fat, gm.			Sugar, gm.	Diacetic acid.	
10.....	84.0	Not recorded.	58	0	640	T.D.2	15.0	0	220
11.....	.....	102	33	0	388	T.D.3	10.0	0	
12.....	.....	64	33	0	252	T.D.4	Trace.	0	
13.....	.....	36	27	0	80	T.D.5	0	0	
14.....	83.6	15	0	0	138	M.D.1	0	0	
15.....	.....	10	11	6	302	M.D.2	0	0	
16.....	.....	22	13	18	440	M.D.3	0	0	80
17.....	82.4	32	24	24	813	M.D.5	0	0	
18.....	.....	52	32	53	1126	M.D.7	0	0	
19.....	81.0	73	51	70					80

<sup>1</sup> Single specimen at entry had 3 per cent. of sugar.

diabetes but also for heart disease and high blood-pressure. The patient was studied according to the Joslin plan, with the result shown in table on page 661.

As can be seen, the patient lost 3 kilograms, or almost 7 pounds of weight, during the ten days he was in the hospital. The urine became sugar free without fasting and acidosis did not develop. The blood-sugar concentration dropped to normal and remained there despite the fact that the diet was increased at a faster rate than is usual. The patient was discharged with a Joslin card and was instructed to increase his diet according to that plan until he developed a trace of sugar or failed to lose a pound of weight per week. He was to continue losing weight and dieting strictly until he had taken off 25 pounds, when he was to report for further instructions. Finally, of course, he was taught to examine his own urine and what to do if sugar appeared, for the educational side of the Joslin treatment is almost as important as any other. On the whole, the result was eminently satisfactory both to the patient and the hospital staff.

#### THE "HIGH FAT" TREATMENT

The so-called "high fat treatment" originates from the work of Newburgh and Marsh, of Ann Arbor, and was carried to its furthest point by Woodyatt, of Chicago. Newburgh and Marsh's first paper on the subject was called "The Use of a High Fat Diet in the Treatment of Diabetes Mellitus" and was published in the Archives of Internal Medicine for 1920, vol. 26, p. 647. Woodyatt's paper, called "The Object and Method of Diet Adjustment in Diabetes," appeared in the Archives of Internal Medicine for 1921, vol. 28, p. 125.

Newburgh and Marsh attacked the problem of diabetic treatment from a purely practical point of view. They conceded the importance of total caloric restriction advocated by Allen, but objected to it on the ground that in order to prevent glycosuria in certain severe cases it was necessary to restrict the total energy so much that the patient became unfit for the ordinary activities of life through inanition. They thought

that such profound inanition might be avoided if the patient were immediately given a low carbohydrate diet with enough calories to maintain metabolic equilibrium. In this way they hoped to clear up glycosuria without fasting and without producing hyperglycemia or acidosis. Accordingly, they investigated the effect of a diet whose energy came largely from fat to which was added sufficient protein to maintain nitrogen equilibrium and the minimal carbohydrate required in making up a diet that a human being could eat over a long period of time. For this purpose they placed their patients when they first came under observation upon a diet containing about 1000 calories, of which 90 gm. was fat, 10 gm. was protein, and 14 gm. was carbohydrate. After the patients became sugar free the diet was increased to one of 1400 calories, of which 140 gm. was fat, 28 gm. was protein, and about 20 gm. was carbohydrate. Finally, a second increase was made, resulting in a diet of 1800 calories, of which 170 gm. was fat, about 40 gm. was protein, and about 30 gm. was carbohydrate. They proved to their own satisfaction in a series of 73 cases so treated that glycosuria was avoided by this method, that acidosis was not precipitated, that nitrogen equilibrium was maintained, and that the patients were able to continue to lead a moderately active comfortable life throughout the entire course of treatment. Therefore they concluded that while doing no harm with the method, they were able to conserve calories and strength for their patients in a way in which the Allen and Joslin methods failed to do. Their contribution, in a nutshell, was to follow out Allen's principles of total caloric restriction, but to modify Allen's plan by substituting for fasting a relatively high caloric diet on which the patients became sugar and acid free, and to discharge their patients upon a maintenance diet containing more calories than Allen or Joslin would allow by giving them a diet balanced not in normal proportions, but with a high proportion of fat and a low proportion of carbohydrate and protein.

Woodyatt attacked the problem of diabetic therapy from a more theoretic point of view and one diametrically opposed to that held by Allen and Joslin. His conception of diabetes is

that the disease is characterized by one single specific defect and that it is not a disease of the total metabolism in the sense of Allen. This specific defect is an inability on the part of the body to utilize as much glucose as may be utilized by the normal body when the supply of glucose exceeds certain limits. The diabetic, however, appears to be capable of utilizing a limited quantity of glucose as well as the normal individual.

Acidosis due to the ketone bodies is not due directly to any impairment of pancreatic function, nor is it an anomaly peculiar to diabetes, but is a secondary effect in the nature of a disturbed metabolic balance resulting from the withdrawal of oxidizing glucose. It appears to be the immediate result of the oxidation of certain fatty acids in the absence of a sufficient proportion of dissociated glucose. Moreover, there is for any given individual at any given time a definite ratio between the quantity of glucose oxidizing in the body and the maximum quantity of fatty acids that can be oxidized in the same time without the appearance of abnormal amounts of the acetone bodies.

The best theoretic treatment of diabetes, therefore, is to bring the quantity of glucose entering the metabolism from all sources below the quantity that can be utilized without abnormal waste, and to adjust the supply of fatty acids in relationship to this quantity of glucose, so that in the mixture of food-stuffs oxidizing in the body acetone bodies shall not be formed. In other words, to rest the pancreas by using a diet of carbohydrates below the point of tolerance, and at the same time to keep up nutrition by using as much fat as can be administered without the development of acidosis.

The method by which Woodyatt estimates the most advantageous diet for any given case depends upon a few relatively simple mathematical manipulations. The first step is to determine the patient's total glucose tolerance, which can be conveniently done by any one of several dietary procedures. The total glucose tolerance, however, is that amount of glucose derived from the carbohydrate, protein, and fat of any diet which can be borne without glycosuria and not merely the carbo-

hydrate figure. This is estimated according to the following formulas:

Let C = Carbohydrate in grams of the diet.

Let P = Protein in grams of the diet.

Let F = Fat in grams of the diet.

Let G = Total glucose in grams of the diet.

$$\text{Formula 1: } G = C + 0.58 P + 0.1 F.$$

Without going into any theoretic details, but attacking the problem from a purely practical viewpoint.

Formula 2: 17 G = the approximate number of calories which any patient with any tolerance can utilize without glycosuria or acetonemia if the diet is most favorably balanced.

The protein fraction is determined arbitrarily. It only remains to estimate the carbohydrate and fat fractions. The carbohydrate can be determined with sufficient accuracy for clinical work by this formula:

$$\text{Formula 3: } C = \frac{8}{10} G - \frac{1}{2} P.$$

And the fat content of the diet is determined by

$$\text{Formula 4: } F = 2 C + \frac{1}{2} P.$$

Thus, from knowing G and P, it is possible to estimate the highest possible caloric diet which any given case can assume without developing acidosis. This diet is Woodyatt's "Optimum Diet" for treatment.

Wilder<sup>1</sup> has introduced an interesting modification of the Woodyatt plan for determining the "optimum diet," which is midway between the Allen rigid diet and the Woodyatt high calory diet. According to his idea the most satisfactory diet for any given case should embody four principles: total dietary restriction; protein restriction; carbohydrate restriction; a balanced diet in fat and carbohydrate to prevent the formation of acetone bodies. This diet is constructed in the following way: the calories of the diet for the patient are estimated from the basal calories required by a normal person of similar age, sex,

<sup>1</sup> Wilder, R. M., Optimal Food Mixtures for Diabetic Patients, Jour. Amer. Med. Assoc., 1922, 78, 1878-84.

weight, and height, and are determined by Du Bois' standards. The protein is restricted to  $\frac{2}{3}$  gram for each kilogram of the patient's body weight for twenty-four hours. The carbohydrate is estimated according to the following formula:

$$\text{Formula 1: } C = 0.024 M - 0.41 P.$$

and the fat by the formula:

$$\text{Formula 2: } F = 4 C + 1.4 P.$$

In these formulas F represents the number of grams of fat, C the number of grams of carbohydrate, P the number of grams of protein, and M the total calory requirement. The calculations for the diet are simplified by nomographic charts.

To give a practical example of how Woodyatt's or Wilder's method can be applied and the difference between them and the Allen or Joslin method, let us take the following case and consider how it might be treated by these various procedures.

The patient (Peter Bent Brigham Hospital, Medical No. 19,664) is a girl twenty-three years old, 5 feet, 5 inches tall, and weighing 112 pounds. Her diabetic symptoms are only of three months' duration, but she has lost 10 pounds in weight and considerable strength. For the past three months she has been drinking a great deal of water and eating a large amount of food. There has been pruritus vulvæ, but no recent infection. Physical examination is negative except for the fact that the Wassermann reaction is strongly positive. She has been treated by the "Joslin Method," with result shown in Table 4.

As can be seen, she has done perfectly well under the Joslin system, reaching Maintenance Diet 8 before showing a trace of sugar on two successive days. The blood-sugar concentration has dropped satisfactorily and acidosis has not developed. We have made a basal metabolism determination, finding that her total metabolism is 24 per cent. below normal, or, in other words, that she needs only 1050 calories to maintain her basal caloric requirements. The problem is what diet to send her home with.

I imagine that Dr. Allen would advise giving her a diet

TABLE 4

Days in hospital.	Weight, kg.	DIET.			Urine sugar, gm.	Blood-sugar, mgm. per 100 c.c.
		Carbohydrate, gm.	Protein, gm.	Fat, gm.		
1.....	52.0	189	89	15	1247	27
2.....	.....	102	58	0	640	55
3.....	.....	64	33	0	388	45
4.....	.....	36	27	0	252	10
5.....	.....	15	5	0	80	8
6.....	.....	15	5	0	80	0
7.....	51.8	10	11	6	138	0
8.....	.....	22	13	18	302	0
9.....	.....	32	24	24	440	140
10.....	.....	42	29	39	635	Trace
11.....	.....	42	29	39	635	Trace
12.....	.....	42	29	39	635	0
13.....	.....	42	29	39	635	0
14.....	51.2	52	32	53	813	0
15.....	.....	63	43	65	1009	Trace
16.....	.....	63	43	65	1009	0
17.....	.....	73	51	70	1126	0
18.....	.....	83	60	88	1364	Trace
19.....	50.0	83	60	88	1364	Trace

much the same as the one advocated by the Joslin plan, provided this was sufficiently low to keep the blood-sugar concentration normal. Dr. Joslin's plan would call for a diet containing about 60 gm. of carbohydrate, 50 of protein (to allow 1 gram of protein per kilogram of body weight), and of 1250 calories (to allow for a minimum of 25 calories per kilogram of body weight). This would be made up from 90 grams of fat. On this diet the patient should remain sugar free, and, barring accident, get along satisfactorily. It would give her enough bulk of food to overcome a too excessive hunger, but not enough energy with which to gain weight or much strength. It would fulfil her caloric and nitrogen balance requirements in a way to prevent any further inanition. It would be reasonably balanced in its proportions of fat and carbohydrate and would not produce acidosis.

The Woodyatt diet for the case would be different. We see that the patient metabolized 73 gm. of carbohydrate, 51 gm. of protein, and 70 gm. of fat without glycosuria. The total glucose of this diet, according to Formula 1, is

$$73 (\text{C}) + 29.6 (0.58 \text{ P}) + 7 (0.1 \text{ F}) \text{ or } 109.6.$$

The patient will be able to tolerate approximately 1860 (17 G) calories by Formula 2 without harm. As to balancing the diet, let us give her 50 gm. of protein or 1 gram per kilo of body weight just as we should according to the Joslin plan. How much carbohydrate can we give her? We determine this by applying Formula 3:

$$87.5 (8/10 \text{ G}) - 25 (\frac{1}{2} \text{ P}) = 62.5.$$

And we obtain the fat of the diet by applying Formula 4:

$$125 (2 \text{ C}) + 25 (\frac{1}{2} \text{ P}) = 150.$$

The Wilder diet would be estimated as follows: Since the patient weighs 50.8 kilograms she only requires 0.66 gm. per kilo or 34 grams of protein each day to maintain nitrogen equilibrium. Her basal metabolism is 24 per cent. below normal; therefore a diet containing the normal number of calories for a girl of her age, weight, and height will actually yield a reasonably

large but not excessive number of calories. This caloric diet, estimated from the Du Bois standard, is 1376. By applying the formulas, we find that the carbohydrate of this diet will be:

$$33 (0.024 \text{ M}) - 13.9 (0.41 \text{ P}) = 19.1 \text{ gm.},$$

and that the fat content will be:

$$76.4 (4 \text{ C}) + 47.5 (1.4 \text{ P}) = 123.9 \text{ gm.}$$

It is interesting to contrast the diets shown on page 670.

As you see, the carbohydrate and protein components of the Joslin and Woodyatt diets are much alike and considerably higher than in the Wilder diet. The Joslin treatment allows 1250 calories, or only 19 per cent more than the basal requirements, the Wilder diet allows 1328 calories, or 26 per cent more than the basal requirements, while the Woodyatt diet allows 1800 calories, or 71 per cent more than the basal requirements. The Joslin and Wilder diets attempt to relieve overstrain of the pancreas by limitation of all the components of the diet, Joslin by a high carbohydrate-protein and low fat mixture, Wilder by a low carbohydrate-protein high fat mixture. The Woodyatt diet attempts to relieve overstrain of the pancreas by limitation of the glucose content of the diet only. The Joslin and Wilder diets are based on Allen's hypothesis that diabetes is a disease of total metabolism, and that tolerance is lost from excess of any kind of food, Joslin deliberately undernourishing the patient, Wilder attempting to substitute with fat the endogenous metabolism which is known to be continuous. Both methods, however, advocate restriction of the total diet as the one essential means for preventing downward progress. The Woodyatt diet is based on the hypothesis that diabetes is not a disease of total metabolism, but one which consists solely in an inability of the body to utilize as much glucose as may be utilized by the normal body. Therefore total restriction of the diet is not necessary so long as the total glucose tolerance of the individual is not exceeded.

This, in brief, is a description of the essential differences

TABLE 5.

JOSLIN DIET. <sup>1</sup>				WOONKART DIET. <sup>1</sup>				WILDER DIET. <sup>1</sup>			
Carbohydrate, gm.	Protein, gm.	Fat, gm.	Calories,	Carbohydrate, gm.	Protein, gm.	Fat, gm.	Calories,	Carbohydrate, gm.	Protein, gm.	Fat, gm.	Calories,
60	50	90	1250	62.5	50	150	1800	19	34	124	1328

<sup>1</sup> In these tables each gram of carbohydrate and protein has been estimated to yield 4 calories, and each gram of fat 9 calories, thus simplifying the arithmetical calculations.

between the Allen, Joslin, and high fat diets of Newburgh, Woodyatt, and Wilder for the treatment of diabetes. One naturally asks which is the best method to follow in the practical management of individual cases.

As I look over my own experience I am struck with the fact that about 80 per cent. of the cases which I have seen were mild and have done reasonably well under any systematic form of treatment. I have come to use the Joslin plan more than any other because it has yielded satisfactory results, because it is systematic, easy to follow, logical, and, above all, because patients can be quickly taught by it how to take care of themselves. The severe cases which I have seen have seemed to yield best results when treated without any rigid system; a method which seemed promising in one case failed in the next. As a general rule I believe that good results can only be obtained in the severest types of diabetes by the physician who is patient, who will pay attention to detail, who will study his case individually, who is well informed about the fundamental principles of acidosis, metabolism, and dietetics, who is versatile and who will modify his course from day to day until he produces an increase in tolerance for a stubborn case by a judicious mixture of all the ideas brought forward by the recent researches in this interesting field.

#### INSULIN<sup>1</sup>

I said that I should speak a few words about insulin. You are all familiar with the history of this drug, and know how it was discovered in Toronto by Banting, Best, and their associates. I shall not discuss its physiologic effect, its method of dosage and administration, or what precautions must be taken when it is being used.

I shall, however, demonstrate a case which has been treated with it for four months. The case speaks for itself and illustrates how much can be hoped for in the future treatment of diabetes. I show this case to enforce a statement made at the beginning

<sup>1</sup> For a summary of the early publications on Insulin see Jour. Metabolic Research, 1922, 2, 125-140. Also see Jour. Metabolic Research, 1923, 2, 547-985.

of this clinic: The advent of insulin will throw upon the hospitals and doctors of this country the burden of treating more diabetics than formerly; the dietetic treatment of diabetics will become no less important thereby. The general practitioner and medical student, therefore, must be more eager than ever to familiarize themselves with the various accepted types of dietetic procedures which, with or without insulin, are at their disposal for con-

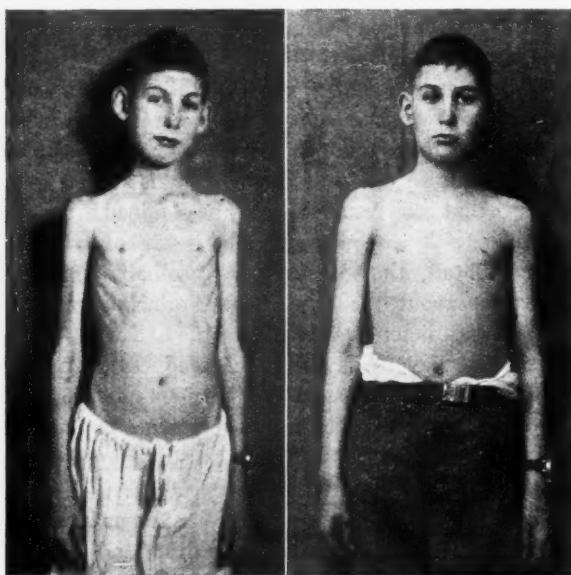


Fig. 105.—Before insulin.

Fig. 106.—Four months after.

trolling any given case. By so doing they will guarantee the future diabetics of the country steadily improving methods of treatment.

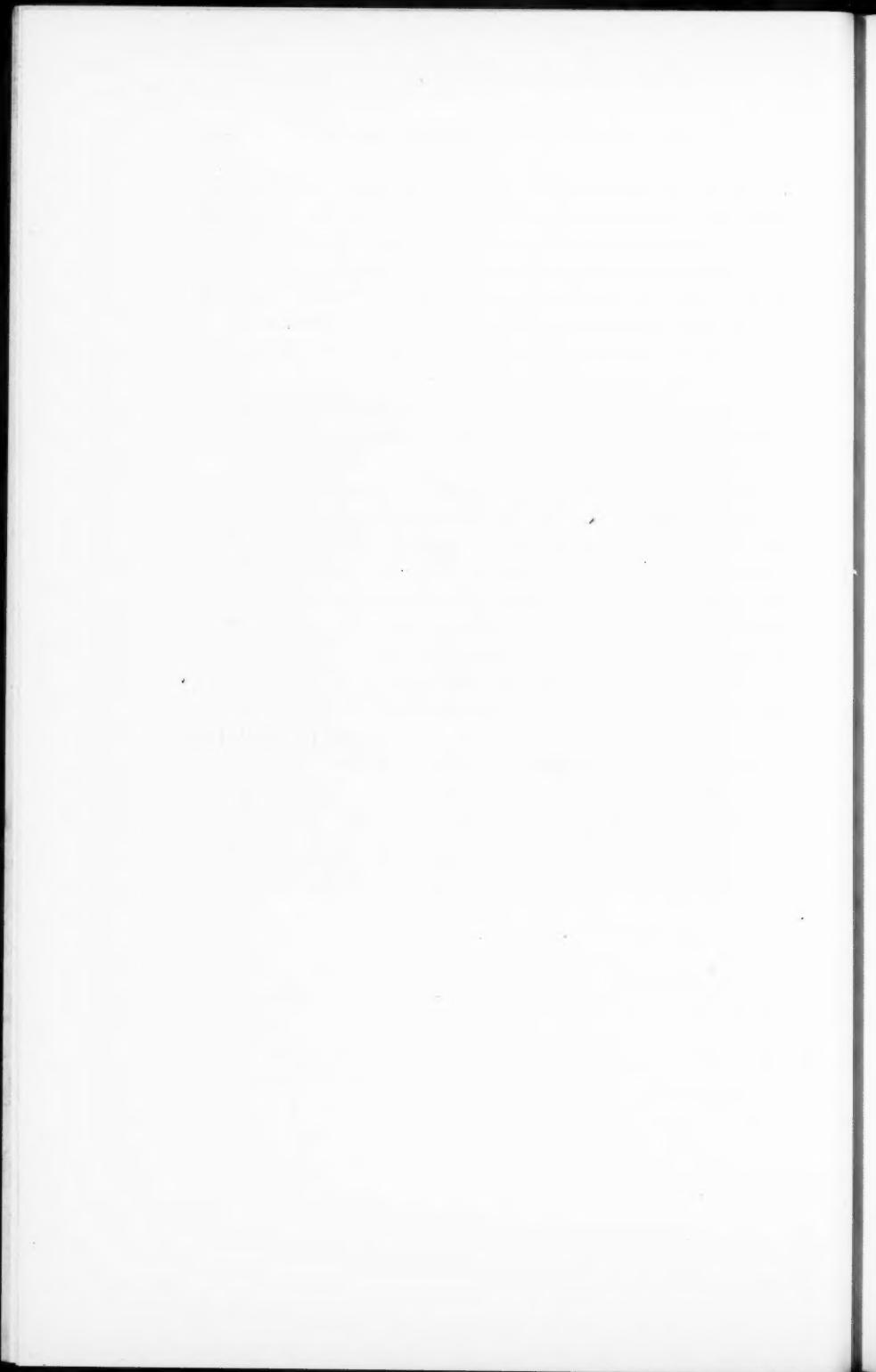
P. B. B. H., Medical No. 20,040, is a boy thirteen years old, who entered the hospital December 11, 1922. He developed symptoms of diabetes about a year ago. Eleven months ago he spent a week in Dr. Joslin's clinic and was discharged with a diet containing 1170 calories. Five months later he again re-

turned to Dr. Joslin's clinic having lost weight and tolerance during the interval and now unable to tolerate more than 1000 calories without glycosuria. During the last seven months he has continued to lose weight and strength and has failed to remain sugar free despite repeated cuts in his diet. Recently he has been eating about 500 calories a day without effect on his glycosuria. He has lost about 17 pounds in weight since the onset of symptoms and 10 pounds during the period of dieting. His physical examination is negative. On the whole, the history suggests severe diabetes in a young boy, becoming progressively worse as time goes on.

At entry to the Brigham Hospital he was given insulin<sup>1</sup> and a diet of 500 calories. His diet was gradually increased until he was finally sent home on a diet containing 2100 calories with a carbohydrate content of 85 grams. Since insulin was started he has gained 19 pounds in weight, has grown an inch in height, has nearly doubled his strength, and, so far as he himself or his family realize, feels normally well and active.

The effect of four months' treatment in this case is well shown by the accompanying photographs (Figs. 105, 106).

<sup>1</sup> The insulin administered to this case was made by the Eli K. Lilly Company, of Indianapolis, under the trade name of iletin.



CLINIC OF DR. HORACE GRAY

NEW ENGLAND DEACONESS HOSPITAL

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BLOOD-SUGAR LEVELS IN DIABETES WHEN FIRST  
SEEN\*

THE influence of the nature and distance of the preceding meal upon the blood-sugar has been extensively reported in the literature, and this, in turn, has been summarized in a previous analytic review.<sup>1</sup> Experts agree on the importance of some standard meal and a standard subsequent interval before venesection if the chemical result is to be adequately interpreted. Yet in private practice the blood so often has been taken in the middle of the afternoon at varying intervals after an unknown meal that these random afternoon blood-sugar tests merit scrutiny, especially in comparison with standard before-breakfast figures.

The purpose of this paper, therefore, is to report a study of blood-sugar determinations on diabetic patients when first seen.

The material has consisted of the histories of 2000 consecutive diabetics seen in this clinic since the routine utilization of blood-sugars began December 10, 1914.

The method of analysis was that of Folin and Wu.

First division may be made into three groups:

(1) 619 cases in which blood was taken at the first office visit, that is, at a random hour, at a varying interval after an unknown meal (hereafter abbreviated as p. c. for post cibum).

(2) 722 cases in which blood was taken at the hospital before breakfast on the morning after admission, usually within a few days of the first office visit (hereafter abbreviated as a. c., ante cibum).

\* From the Service of Dr. E. P. Joslin at the New England Deaconess Hospital, Boston.

(3) 659 cases in which blood was taken either not at all or not until some time (arbitrarily three days) after the beginning of treatment. Obviously that group must be omitted from this study of admission status.

**Comparison of P. C. Average with A. C. Average.**—0.19 vs. 0.21 per cent. The cause of this surprisingly low result in the afternoon was in part (1) our habit in the office of postponing the blood-sugar on any patient sick enough to be sent on to the hospital, a habit, therefore, which meant exclusion of many severe cases from the p. c. group; and (2) neglect in many of the earlier cases to record the interval since the last meal, a neglect which meant the inclusion in the p. c. group of a certain number of bloods taken four or five hours after eating.

A suggestion from the low result is that casual p. c. values, however useful at times for transient patients, are of less permanent value, and hence do not indicate with any great accuracy the severity of patients seen in any particular clinic. Judged by a p. c. value, interval not stated, a patient who had been seen at 2 p. m. would seem sicker than a patient seen at 5 p. m., which is preposterous; and, even with the intervals stated, p. c. values can be tabulated for study only with an inconstant factor not present with before-breakfast values.

The relative frequency of occurrence of the different levels of blood-sugar on admission is put on record in Fig. 107. The following features may be considered:

1. The large number of low B. S. If we consider a. c. and p. c. together, we find values of 0.20 g/100 c.c., or less, in 59 per cent. of the 1341 cases. If we consider 0.11 a. c. as the highest normal, we find 17 per cent. of the a. c. values normal. If we regard 0.16 p. c. as the highest normal, we find 54 per cent. of the p. c. values normal. In other words, according to p. c. values more than half our diabetics had normal B. S., hence the labor of these blood determinations was of notably less significance as compared with a. c. values, which were abnormally high in more than four-fifths of the cases. This is not to claim that a normal blood-sugar, whatever the time, is useless; it is very cheering.

2. The moderately elevated range usually found in the untreated diabetic needs little comment. Values from 0.21 to 0.30 inclusive, and considering a. c. and p. c. together, occurred in 26 per cent. of the 1341 cases, and from 0.31 to 0.40 in 12 per cent.

3. Severely elevated values—*i. e.*, above 0.40—occurred in 43 cases, or 3 per cent., of all the 1341 cases studied. The two highest were 0.57 and 0.58. This group is probably small enough to

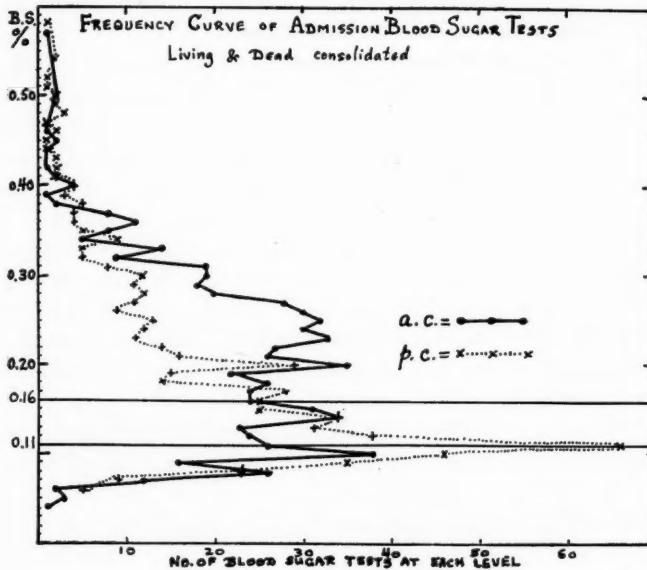


Fig. 107.

merit special study at some later time, with particular attention to such elevated values occurring once on admission, then falling promptly to normal and remaining so for considerable periods.

4. Extraordinary values, that is, 0.60 or over, certainly merit case reports. In this series there was one such value, 1.37, which has been reported by Dr. Joslin in 1916.<sup>2</sup> It seems wisest to make an exception for this instance by omitting it from the averages and from the total of 1341. As a matter of

interest the other extraordinary values (though some possibly were not taken at first visit) which I have so far found in the literature may be assembled here: 1.36 (Baudouin<sup>3</sup>), 1.28 (Höst<sup>4</sup>), 1.20 (Blum<sup>5</sup>), 1.15 (Cohen<sup>6</sup>), 1.10 (Myers and Bailey<sup>7</sup>), 1.07 (Newburgh and Marsh<sup>8</sup>), 1.06 (Lépine<sup>9</sup>), 1.02 (Black<sup>10</sup>), 1.01 (Von Noorden<sup>11</sup>), 1.00 (Campbell<sup>12</sup>, Marsh<sup>13</sup>, Petty<sup>14</sup>), 0.98 (Myers and Bailey), 0.95 (Weiland<sup>15</sup>), 0.90 (Heppe-Seyler<sup>16</sup>), 0.84. (Fitz<sup>17</sup>), 0.80 (Cantani<sup>18</sup>, Myers and Bailey), 0.79 (Weiland, Myers and Bailey), 0.78 (Tachau<sup>19</sup>), 0.77 (Weiland), 0.76 (Rogers<sup>20</sup>), 0.71 and 0.66 (Weiland).

**Mortality in Relation to Initial B. S.**—The proportionally worse prognosis the higher the admission blood-sugar is patent. If among the patients at each B. S. level we reckon the percentage now dead, we see the law in the serial figures of Table 1 (a. c. and p. c. together) and in Table 2 (a. c. alone). If we try in Table 3 to refine the curve by making averages for every 5 instead of 10 points B. S. (centigrams per 100 c.c.), the curve remains smooth for a. c., but not for p. c. values. The high extremes, 0.40 per cent. and over, have to be consolidated owing to the relatively small number of observations. The blood-sugar thus forecasts the future with an accuracy which has not been demonstrated for urine sugar.

In the light of these mortality tables we must reconsider the averages given in the early part of the paper: 0.19 g/100 c.c. p. c. vs. 0.21 a. c. The reader may remark that the difference is only 0.02 g/100 c.c. or 10 per cent., that is, almost within the limits of error of bedside chemistry in practice, so why this insistence on the importance of a. c. tests? In reply:

1. This apparently inevitable reasoning neglects the well-known drawback of averages: individual case characteristics often negative one another and become lost in the mass. To be specific, the averages 0.19 and 0.21 do not represent the extent of difference in the individual cases. Not two (2) points but seven (7) is nearer the truth. This is evidenced by the blood-sugar on 2 patients (Nos. 2590 and 2998), secured both at the office in the afternoon and the next morning before breakfast at the hospital. The figures were 0.24 and 0.27 p. c. vs. 0.18

and 0.19 a. c. Referring to Table 1, what prognosis could be given these two patients? Suppose only the afternoon blood had been taken, then they would fall in the group of which 28 per cent. are now dead. But, fortunately, their fasting figures were secured, thus placing them in another group, whose mortality was precisely half as great. If you, reader, should discover tomorrow that you were diabetic, would you take the trouble to visit your physician before breakfast?

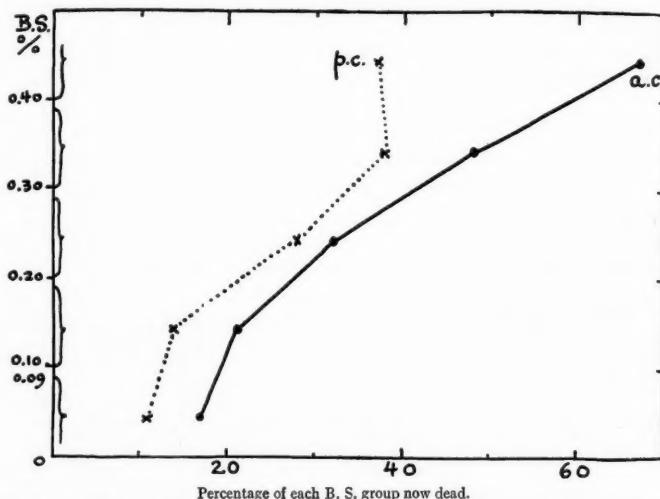


Fig. 108.—The higher the initial B. S., the higher the mortality rate. Note smoother progression of a. c. curve.

2. Differences so small as to be insignificant in a single case may not infrequently be significant when they concern averages.

3. The progressively higher mortality rates with higher admission blood-sugar levels is shown graphically in Fig. 108. Parallelism is clearer in the a. c. curve, plotted from Table 2, than in the p. c. curve, which is, therefore, not tabulated.

TABLE 1

*Mortality Among 1341 Diabetics Grouped by Admission B. S., a. c. and p. c.  
Together*

B. S. g/100 c.c.	0.09 and less	.10-.19	.20-.29	.30-.39	.40 and over
Total cases.....	131	594	417	156	43
Number dead.....	14	82	116	60	16
Dead percentage of total..	11	14	28	38	37

TABLE 2

*Mortality Among 722 Diabetics Grouped by Admission Blood-sugars, a. c. Only*

B. S. g/100 c.c.	0.09 and less	.10-.19	.20-.29	.30-.39	.40 and over
Total cases.....	60	272	279	96	15
Number dead.....	10	56	88	46	10
Dead percentage of total..	17	21	32	48	67

TABLE 3

*Same as Table 2 but in Greater Detail*

B. S. g/100 c.c.	0.09 and less	.10-.14	.15-.19	.20-.24	.25-.29	.30-.34	.35-.39	.40 and over
Total cases.....	60	145	127	151	128	66	30	15
Number dead.....	10	23	33	45	43	30	16	10
Dead percentage of total	17	16	26	30	34	45	53	67

**Living vs. Dead.**—The fatal averages were, as expected, higher. The number of cases to each average are given in parentheses.

	Per cent. a. c.	Per cent. p. c.	Percent. a. c. and p. c.
Dead.....	0.24 (210),	0.23 (78),	0.24 (288)
Living .....	0.19 (514),	0.18 (541),	0.19 (1053)

**By Ages.**—Adolescents showed values like adults, but children under ten completed years did exhibit lower figures than adults, a fact which is always a fresh surprise each time one hears it because of the notorious severity in the first decade.

	Per cent. a. c.	Per cent. p. c.	Per cent. a. c. and p. c.
Adults.....	0.21 (617),	0.19 (557), or	0.20 (1174)
Second decade.....	0.21 (70),	0.18 (50), or	0.20 (120)
First decade.....	0.19 (36),	0.16 (13), or	0.18 (49)

**Duration of Diabetes from First Visit to Death.**—The feasibility of predicting from the admission blood-sugar the length of life ahead of a patient is a most important consideration. The lower the initial fasting blood-sugar, the longer the ex-

pectation of life, would be our hope. It appears to be true in Fig. 109, which is offered tentatively, and will be brought up to date as soon as the fatal a. c. figures grow from 210 to a satisfactory statistical size. A disappointingly short life is seen in the average of 1.6 years for the group 0.09 and under (and is not altered if we recalculate, using 0.11 as the dividing line). This average if eventually confirmed would necessitate amending the above rule to the extent that, while the expectation is

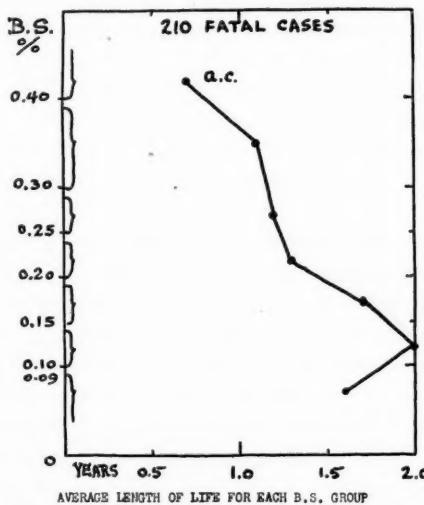


Fig. 109.—The higher the admission B. S., the shorter the expectation of life.

best for B. S. of 0.19 or less, it is no better for values strictly normal. That this average, however, is unduly low and may well be increased later, seems a reasonable hope in view of three facts:

1. The group at present numbers only 8 cases.
2. The course of fatal cases in general has increased from 3.3 years for the period 1895-1913 to 5.3 years for 1920. Patients with low admission B. S. might fairly be expected to exceed the average expectation of life.

3. The cause of death were respiratory infections in 5 instances (definite pneumonia in No. 1453, tuberculosis in No. 1319, and influenza in Nos. 1401, 1454, 1477) and coma in only 3 (Nos. 923, 1200, 1695). In these 3 coma cases of acutely progressive diabetes the patients were, as the reader may guess, all young children; in them the disease had begun at 3.8, 8.8, and 12.8 years, and the course after first visit lasted respectively 1.2, 0.8, and 4 years.

Prior treatment as a possible explanation of the low admission B. S. can be postulated only in No. 1453, who died of pneumonia without coma.

Regarding this phenomenon of normal B. S. in fulminating cases in children Dr. Joslin has written: "Their course in the hospital was by no means as favorable as such low percentages would imply. Their future behavior will be watched with much interest."

**By consecutive hundreds of patients seen**, all ages together, the admission blood-sugar shows a slight rise, which may be attributed to growing severity of the disease, which is unlikely, or to increasing knowledge of the disease on the part of the general practitioner, so that he refers patients less often in milder stages. The closeness of the a. c. and p. c. curves in the region of the latest 500 cases suggests the existence of a new factor, which, however, I cannot explain. (See Fig. 110.)

The upward trend of the fatal curve in the latter half of the period considered may be described by the statement that whereas the admission B. S. a. c. of the patients now dead used to average 0.22, it now averages 0.29 per cent. The corresponding averages for the patients now living come to 0.17 and 0.21. In other words, a patient with fasting B. S. equal to the former fatal average, would today nearly meet the average for the living.

In successive hundreds of patients seen, the percentage to have an admission blood-sugar done ran as follows:

10-26-38-46-56-55-69-77-62-68-66-74-/

83-88-94-92-89-88-76-86 per cent.

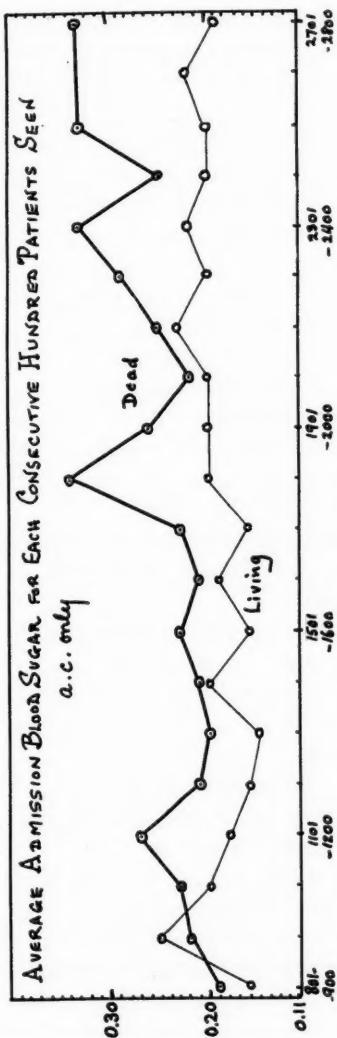
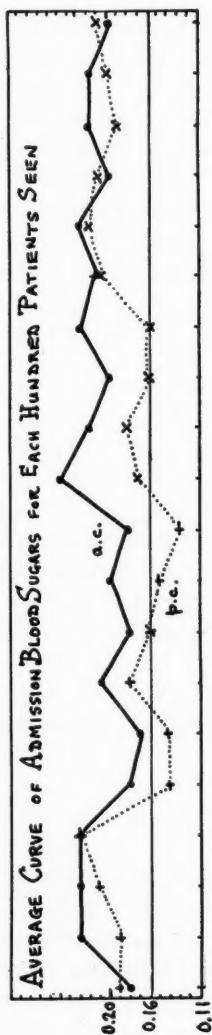


Fig. 110.

This increase, especially in and after the hundred starting with 2001, admitted November 29, 1920, is in the right direction.

Among the blood-sugars done in each hundred, the percentage to have the determination done a. c. ran as follows:

80-39-63-74-84-76-71-67-66-69-50-43-

52-35-54-41-47-33-41-44 per cent.

This decrease in the usage of the postabsorptive value represents a tendency which probably should be combated, remembering, on the other hand, the importance, whenever the blood-sugar a. c. is normal, of securing a test half an hour or an hour after a standard carbohydrate meal. This necessity arises most often in the following circumstances:

1. Renal glycosuria.
2. Pregnancy glycosuria.
3. And, most important, true diabetes mellitus so well treated that the a. c. blood-sugar is normal. But that is generally another story, viz., treatment. The present paper deals only with blood-sugars taken on admission, *i. e.*, for diagnosis and prognosis.

**Conclusions.**—The admission blood-sugar of a diabetic or suspected diabetic might well be governed by the following theses:

1. If diabetes is fairly certain from the history and from glycosuria of more than 1 per cent., then the postabsorptive blood-sugar (before breakfast, or after as long a delay after the preceding meal as can be arranged) is indicated, because:

(a) The lower the B. S. can be caught, the more optimistic the verdict the physician can give. Prognosis from urine sugar is less established.

(b) The B. S. a. c. is the most useful for further statistical and comparative studies.

(c) Diagnosis of diabetes was confirmed by abnormal values in 83 per cent. of the a. c. B. S. tests vs. only 46 per cent. of the p. c. tests. It must be granted that this latter figure can be much improved by keeping record of the interval p. c. and the kind of meal eaten; in this respect, as in others, we are constantly aiming at greater precision.

2. Conversely, if a renal or a mild glycosuria seems pos-

sible from lack of symptoms and from less than 1 per cent. of sugar in the urine, then the p. c. B. S. is more desirable than the a. c. value. But one should avoid taking the blood at random. Remembering that blood-sugar analysis costs more, and is worth more, the patient may well spend the time to eat a known carbohydrate load (glucose 100 gm., or bread 50 gm., or two shredded wheat biscuits and a half-glass of milk) in the office and have the blood taken after a half-hour, and the urine simultaneously. Better still, if the patient live near enough, is a brief visit to the office the next morning half an hour after eating whichever of the named breakfasts the physician habitually uses.

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## CLINIC OF DR. EDWIN A. LOCKE

BOSTON CITY HOSPITAL

### OSTEOMALACIA (JUVENILE FORM)

THE case which I shall demonstrate to you, although somewhat of a rarity, is of unusual interest. The history which we have obtained from the parents of the child is very meager and unsatisfactory.

This little colored girl is fourteen years old, and entered the hospital February 2, 1922 because of the deformities in the legs and severe convulsions.

**Family History.**—Father living and well. There is no history or evidence of any physical abnormalities. Syphilis denied. Mother never robust. There is an apparent difficulty in the use of the legs, especially when she goes up and down stairs. She has had only one other pregnancy; child died at three of "rickets and heart disease."

**Personal History.**—At birth the baby is said to have been absolutely normal, but within a few weeks developed a persistent nodding movement of the head which was present continuously except when sleeping. This lasted for about a month, then ceased, and never recurred.

She was nursed for one year, seemed to gain normally in weight, and was considered perfectly well. No illnesses occurred during this period. The exact time at which the first teeth appeared is not known, but the mother thinks at about the end of the first year. The parents cannot recall when she first sat up, but are confident that she began to walk at two years, and nothing abnormal was noted. When three or four the parents first observed that the legs were deformed. The child was "knock-kneed," but could, nevertheless, walk without great

difficulty. The deformity was slowly progressive. At the age of six the changes in the legs were very marked, and at about this time a slight deformity of the wrists was also noted. The changes in the arms and legs have continued to progress. Since the age of eight she has been unable to stand or walk without the aid of crutches.



Fig. 111.—Osteomalacia. Female, age fourteen years.

Pain in the legs has been a somewhat prominent symptom. On at least two or three occasions she has injured one or the other of her legs by falling. These injuries, however, have laid her up for only a few days.

The child has never attended school, but the parents feel that she is normal mentally. No illnesses except as mentioned above.

Menstruation began at thirteen. It has always been regular, without much pain, and a normal flow which lasts four days.

Approximately three years ago she had two or three mild convulsions lasting a few minutes. These were always of short duration, and until a few months ago recurred only at very long intervals. Of late they have become an almost daily occurrence, and during the past few weeks sometimes as many as two in a single day. The duration and the severity have markedly increased. From the description given by the mother it is evi-



Fig. 112.—Osteomalacia. x-Ray of right leg of patient shown in Fig. 111. Note the very marked atrophy of the bones, the bowing, and the numerous partial and complete fractures.

dent that the chief feature of the attacks is a more or less generalized tonic spasm. The joints of the upper extremities are evidently flexed and held rigidly. The toes are strongly flexed; the feet turned inward, the knees pressed together and flexed. She cries out with pain and perspires profusely as if in great agony. Consciousness is never lost, the tongue is never bitten, and there is no incontinence. Recently the duration of the convulsions has been about a half-hour. Great prostration follows these seizures.

**Physical Examination.**—In general, you will see that the child is well nourished, but very undeveloped physically. While she seems moderately alert and observant, there is a very obvious lack of mental development. She is very restless, apprehensive, and so sensitive to the touch of the examining hand that a thoroughly satisfactory examination is impossible.

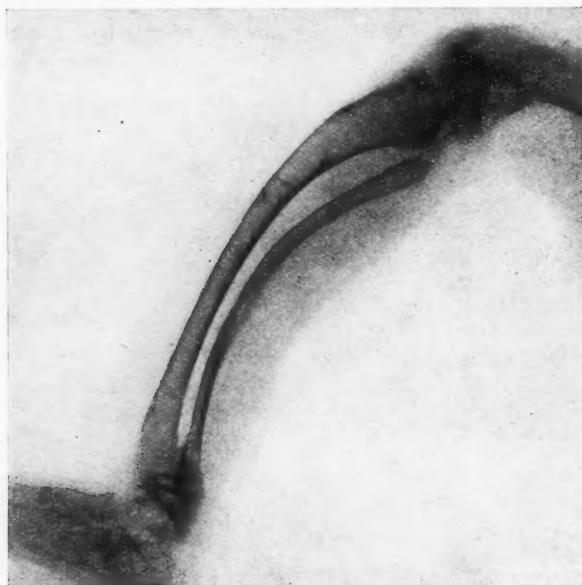


Fig. 113.—Osteomalacia. x-Ray of left leg of patient shown in Fig. 111.

The eyes are normal. The teeth are more or less generally malformed and the canines and incisors are irregularly spaced, but with no evidences of the Hutchinsonian type. The tongue when protruded shows a fine tremor.

A fairly definite tonic condition of practically all the skeletal muscles is shown, and you will observe their very striking mechanical irritability. Chvostek's sign is present. The deep reflexes are exaggerated. To a varying degree all of the joints are flexed and resist any attempt at extension.

Most striking are the gross deformities. The head is large, all of the diameters of the cranium being increased. The cranium is symmetric, smooth, and presents no irregularities. In comparison, the face seems small, but is otherwise normal.

The chest, though symmetric, is very abnormal. The shoulders are rounded and the thorax is depressed in front. A slight suggestion of a bilateral Harrison groove and rosary is present. The abdomen is rounded and moderately protruding.

Except for the lack of normal muscular development the arms present no striking abnormalities. There is a slight suggestion of bowing in the forearms. The wrists are flexed to nearly a right angle with pronation and cannot be fully extended. The epiphyses feel a trifle enlarged in comparison with the very slender shaft of the long bones. Considerable limitation of motion exists in all the joints of the upper extremities. Both legs, on the other hand, are grossly deformed throughout, the most obvious change from the normal being a broad anterior bowing. In consequence of the eversion of the feet there is an appearance of marked lateral bowing also. The feet are held in such position that the soles approximate each other. Marked flexion in all the joints of the legs is present and the patient strongly resists any attempt at extension. The pelvis is malformed chiefly, it seems, as a result of ventral compression which has forced the symphysis backward. The great trochanters are slightly above Nelaton's line, suggesting bilateral dislocation of the hips. The epiphyses seem large, and in the upper portion of the shaft of the right tibia is a very marked bony irregularity probably the seat of a malunited fracture. The shafts of the long bones of the legs are very small, evenly curved, and smooth.

The urine, stools, and blood are normal; Wassermann test negative.

As you will see from the chart, there has been a slight temperature varying from 99° to 100° F. throughout her stay in the hospital. The pulse has been more irregular, but, as a rule, somewhat above normal.

**x-Ray Report** (Dr. Honeij).—The bones appear to be those of a young adult, showing poor development with definite deformities and abnormal processes. The vertebrae are of the juvenile type, while the long bones represent the adult type.

*The Skull.*—The inner diameters of the skull are increased. The anteroposterior diameter is 19 cm. and the greatest perpendicular diameter is 14 cm. (base to vault). The tables are not uniformly increased in thickness; the posterior portions are markedly thickened, being 2 cm. in its greatest and 1 cm. in its thinnest portion. The frontal portions vary from 0.4 to 1.2 cm. in thickness. The circulatory depressions are unusually prominent at the base of the skull. The mastoid portion is small and not as heavy as usual. The sella turcica is shallow, flattened, and poorly defined. The sinuses are small.

The bones of the face are poorly developed. The teeth are well developed, but irregular in shape and position.

*The Pelvis.*—The pelvis is asymmetric, narrowed, with a greater vertical plane than is usual. It is poorly developed. All the bones have a spongy appearance, irregular in density, and rarefied, indicating a marked diminution of lime salts (halisteresis). The outlines of the bones are fairly distinct.

*The Femora.*—The heads and trochanters are large, semi-rarefied (halisteresis), with irregular densities. The heads are flattened and poorly defined. The necks and trochanters are well outlined. The angle is correct. The epiphyseal lines are barely discernible. The femora are approximately 27 cm. in length, and varying in width from 1.8 to 3.2 cm. The shafts are curved inward and forward. The corticalis is thin, but fairly well defined. The canal is almost transparent and widened. In the middle of both shafts there is an area of irregularity which suggests old fractures; this is especially so on the right. The condylar portions are rather large, quite deformed, with scarcely perceptible epiphyseal lines, rather rarefied (halisteresis), and with definite indications of a supracondylar fracture with some displacement. There is little to indicate the amount of callus formation, which probably was slight. The patella on both sides is small. The knee-joint space is narrowed.

*The Tibiae and Fibulae.*—The length of the tibia is approximately 28 cm., the fibula 25 cm., with marked curving outward and forward. The heads of both tibiae are flattened and poorly developed. The epiphyseal lines, upper and lower, are barely discernible. The corticalis is thin, but well defined. The lower ends of the bones show some penciling. The fibulae show some compensating thickening in their middle portions. There is evidence of transverse fractures near the lower epiphyseal lines of both bones of both legs. The joint spaces are narrowed.

*The Feet.*—The bones of the feet are irregular in form, somewhat flattened, well outlined, but more or less rarefied (halisteresis).

*The Vertebrae.*—The vertebrae are small, somewhat flattened, but approach the normal more than any of the other bones. There is a very slight double curvature. There is no evidence anywhere—except in the bones of the skull—of the presence of new bone formation or hypertrophic processes.

**Diagnosis.**—Someone has suggested the possibility of congenital syphilis in this case. There is no evidence from the family history of an antecedent form of this disease, neither have any typical syphilitic lesions been found on examination. The Wassermann test is negative. Finally, the bone lesions described do not correspond with those characteristic of congenital lues.

The disease of the skeleton exemplified by this case bears no resemblance to osteopetrosis (osteogenesis imperfecta), but the question has been asked if this is not an example of this affection. Osteopetrosis is almost always congenital. Its chief characteristic is a striking deficiency in the bony development leading to multiple fractures of the long bones, especially those of the arms and legs. In some instances several hundred fractures have been counted. In consequence of the great fragility of the bones and the resulting fractures, the bones present an absolutely unique outward appearance. They are extraordinarily misshapen, with sharp angulations and curves. The most unique feature of the deformity, however, is the pres-

ence of very numerous angular ridges due to callus formation. Because of these, it has been likened to a bamboo rod. You will in this case note the entire absence of such characteristics either on palpation or in the radiograms.

The diagnosis seems to lie between rickets and the infantile type of osteomalacia. A differentiation between these two diseases in childhood is not always easy and, indeed, by many the two are considered identical. In both diseases the outstanding features, so far as the osseous system is concerned, are softening and deformity. Many careful studies, however, in recent years have established juvenile osteomalacia very positively as distinct from rickets, although there are many pathologic and clinical features common to both. The especial osseous changes distinctive of rickets are the striking changes in the head and the epiphyses. The most common characteristics of the skull consist in thickening of the frontal and parietal eminences, with flattening of the vertex, giving a box-like form, the so-called "hot cross-bun" head. In very young children particularly certain of the cranial bones are sufficiently softened to be compressible (craniotabes). Various other and less common abnormalities occur. None of these deformities are found in this case. Instead the cranium shows an even, symmetric enlargement throughout. The epiphyseal characteristics of rickets are the result of very pronounced enlargement of the bones at these points, most noticeable in the long bones and especially the radius. The distal epiphyses are chiefly affected. The costochondral enlargement gives the rachitic rosary. Here again in our case such features are absent. Mention is made in the physical examination of a suggestion of a rosary and of slight enlargement of the epiphyses of the long bones, but both are so slight as to be without real significance, as you will see. Furthermore, the radiograms also fail to show these essential lesions of rickets. On the other hand, the whole clinical course, the deformities, and the *x*-ray appearances in the bones are typical of osteomalacia. These especial features of osteomalacia will be discussed in some detail later. In brief, we have an example of a disease of a chronic progressive type, much more

common in females, especially characterized clinically by severe constant dull pain, muscle weakness, and deformity resulting from bending and fractures of the bones. The essential lesions are confined to the skeleton and consist of a generalized softening and absorption of bone (halisteresis) accompanied by the production of new and uncalcified osteoid tissue.

**Clinical Types of Osteomalacia.**—The disease may be divided into several types according to the age period at which it occurs, and especially with reference to its appearance following pregnancy. Clinically, osteomalacia shows a relatively constant picture in these different groups. In their order of frequency these forms are:

1. *Puerperal Form.*—The disease is seen most commonly with pregnancy or during the period of lactation. In one series of 132 cases collected from the literature, 91 were observed in women during pregnancy. It seldom occurs in primiparæ, but appears to develop most frequently in women who have numerous and frequent pregnancies. At first the affection may be mild and all symptoms disappear after lactation, to reappear in a more pronounced form with each succeeding pregnancy. Remissions and exacerbations which are particularly characteristic of this form are scarcely ever observed in the remaining groups.

2. *Non-puerpural Adult Form.*—A mild type is occasionally met with in women unassociated with either pregnancy or lactation, and with about equal frequency in men. An important feature in these cases is the fact that the involvement of the pelvis is much less marked. Furthermore, the skeletal changes are apt to be more generalized.

3. *Senile Form.*—Osteomalacia with a gradual onset, relatively mild and very prolonged course has been recorded in a few instances in the later decades of life. The changes in the bones are wide-spread and the pelvic alterations are not prominent. This condition is often confused with osteoporosis so common in old age. In the latter the deformities are relatively slight unless resulting from fractures, and flexibility of the bones is wanting.

4. *Juvenile Form.*—Most rare of all is the type seen in children at about the time of adolescence. It is said to follow trauma, and especially the infectious diseases. The condition is often confused with rickets, and especially as the two diseases may coexist in the same child. Much confusion has until recent years existed regarding the relationship of infantile osteomalacia and rickets. By many the former has been considered as a form of late rickets. Troussseau and Lasègin have contended for the unity of the two. In recent years, however, Virchow and his followers have insisted on a sharp separation of osteomalacia and rickets, and their position seems well established.

Tetany is a very common manifestation.

5. *Hunger Osteomalacia.*—During the past few years, namely, since the Great War, an enormous number of cases of generalized bone softening with clinical features closely resembling if not identical with osteomalacia have been observed in Austria, and to some extent in Germany. Through the early years of the war these cases were a rarity, but in 1919 and 1920 were seen with extraordinary frequency. In Vienna, especially during 1920, the disease assumed an "explosive form." Schiff<sup>1</sup> reports having seen 60 cases in his clinic during a period of two weeks, among whom were 20 men. Alwens<sup>2</sup> treated 26 cases in his wards during a period of three months in 1919. Over 600 cases visited Prof. Schiff's Clinic in Vienna between January, 1919 and May, 1920.<sup>3</sup>

The patients were almost exclusively from the poor and most destitute classes. No age was exempt, but those of both sexes beyond the middle period of life were much more commonly attacked than in true osteomalacia. The association with pregnancy was likewise less striking. Males have seemed much more resistant than females. The frequency with which several members of the same family are affected with the disease has led to the adoption of the designation "familial hunger osteo-

<sup>1</sup> Wien. med. Wchnschr., 1919, lxix, No. 13, S. 649.

<sup>2</sup> München. med. Wchnschr., 1919, No. 38, lxvi, 1071.

<sup>3</sup> Dalyell, The Lancet, 1921, 11, 842.

malacia" which so often appears in German literature of the past few years. Tetany is a common symptom.

A very spirited discussion has taken place in the German medical literature as to the relation of this disease to true osteomalacia. Schlesinger,<sup>1</sup> for example, argues that the affection is to be regarded as only similar to osteomalacia inasmuch as its frequency, rapid development, its appearance in elderly, mentally normal men, the adrenalin glycosuria, and the general immunity of the pelvic bones make it improper to include it in the group of ordinary bone-softening diseases. In other respects, however, the clinical picture conforms to the general symptomatology of osteomalacia, and a careful study of the reported cases and discussions leaves me with the conviction that the so-called "hunger disease" is a form of osteomalacia.

That the malady is in some way dependent on nutritional disturbances is clear, as its appearance is invariably in those individuals who are greatly impoverished. It is difficult to go beyond the point of stating that it is a disease of under-nutrition. Sauer<sup>2</sup> suggests that the undernutrition results in a suppression of the function of the parathyroid glands, which, in turn, leads to a disturbance of lime metabolism resulting in a malacia of the bones. The theory that the disturbance in bone metabolism results from a dysfunction of the glands of internal secretion has many ardent advocates. Schlesinger<sup>3</sup> says that hunger osteomalacia may be connected with a diet deficient in fat. Porges,<sup>4</sup> on the other hand, is of the opinion that the disease is not due to a lack of fat, but albumin. Again, Alwens<sup>5</sup> concludes that the cause is to be found in a lack of albumin, lime, and phosphorus.

Very generally the response to treatment in hunger osteomalacia is prompt and satisfactory. In many recorded cases the giving of a full normal diet has been followed by immediate improvement, and in a comparatively few weeks complete re-

<sup>1</sup> Wien. med. Wchnschr., 1919, No. 16, lxix, S. 799.

<sup>2</sup> Deutsch. med. Wchnschr., 1919, xlvi, S. 1373.

<sup>3</sup> Wien. klin. Wchnschr., 1919, No. 37, S. 929.

<sup>4</sup> See Schlesinger, Wien. med. Wchnschr., 1919, lxix, No. 35, S. 1710.

<sup>5</sup> München. med. Wchnschr., 1919, lxvi, No. 38, S. 1071.

covery is often seen. Relapse, however, is the rule if the patient is allowed to return to the insufficient diet.

*Osteomalacia in Animals.*—Osteomalacia occurs in all domestic animals, but primarily among those which lead a stall life. Its frequency varies with localities, being most common among the cattle in central Europe, and especially in Moravia and Austria. One author estimates the number of cattle attacked in lower Austria alone as 16,000. A very hot and dry season with resulting scarcity of fodder is regularly followed by an outbreak of the disease. Wild animals living in their native state are never, so far as known, subject to the disease. It is the general opinion that osteomalacia in animals is due to a lack of lime in the food, and this view has received substantial support by repeated successes, experimentally, in producing the disease by feeding cattle with fodder poor in calcium salts.

**Etiology.**—While no age is exempt, osteomalacia is essentially a disease of early adult life, a distinct majority of cases developing between the ages of twenty and thirty. Its occurrence at the extremes of life is very rare.

The relation of the disease to pregnancy is a very definite and interesting one, yet the exact etiologic significance of gestation is not fully understood. As I have already stated, osteomalacia almost never appears in primiparæ, but in women with frequent pregnancies, an exacerbation of the disease often occurring with each gestation. Because of this association sex is an important consideration, females comprising about nine-tenths of the cases.

As is apt to be the case in diseases of unknown etiology, there are many theories as to the cause. The disease is much more common in individuals from the poorer classes, and there seems sufficient evidence for assuming that it bears some relation to bad hygienic surroundings and insufficient or poorly balanced diet. Proof of this exists in the prevalence of cases in Austria and Germany following the war, and obviously in some way resulting from the extreme undernutrition. Osteomalacia, however, does occur among well-to-do individuals whose nutrition and general health seem perfectly normal.

That some particular and unknown food deficiency may be a cause is suggested by the fact that the malady is known to be very prevalent in certain limited localities. Feeding experiments in animals have repeatedly shown that extensive osseous changes identical with those found in osteomalacia can be produced by a diet from which calcium is excluded. Similar experiments in man have been uniformly inconclusive. It therefore seems a reasonable conclusion that while severe and prolonged nutritional disturbances undoubtedly may play a part, and perhaps an important one, other factors must be sought for.

Since osteomalacia is often a sequel of some infectious disease, and since the changes in the bones as well as the clinical course of the disease are such as may occur when the bones are invaded by infectious organisms, the opinion has been held by many that the bone changes are due to the presence of micro-organisms. On the whole, the evidence is strongly against this theory.

A favorite and much-discussed theory is that the disturbance in the bone metabolism is due to dysfunction of one or more of the endocrine glands. There is considerable evidence to support this idea, but I shall only mention a few facts by way of illustration. Bone changes often accompany diseases of the thyroid gland. Considerable success has followed the administration of adrenalin in cases of osteomalacia. There is good evidence, furthermore, that the adrenalin secretion influences bone metabolism. Attention has been especially directed to the ovaries by the successful treatment of osteomalacia by oöphorectomy. Fochier in 1879<sup>1</sup> observed a complete cure of osteomalacia in a woman on whom hysterectomy and oöphorectomy had been done at the time of cesarean section. This author and Fehling,<sup>2</sup> later, reported brilliant results in cases treated by this method. Unfortunately for this theory it seems reasonable as suggested by McCrudden that the good results observed may not have been the direct result due to the

<sup>1</sup> Lyon méd., 1879, xxxi, 393, 473, 505, 545.

<sup>2</sup> Arch. f. gynæk., Berlin, 1891, xxxix, 171.

removal of overactive ovaries, but indirectly to the prevention of further conception. Again, it has been conclusively proved that castration is without effect on the general metabolism.

The careful metabolic studies in osteomalacia made by McCrudden seem to offer a real basis for a satisfactory explanation of the bone changes. His results show a constant increased excretion of calcium and an equally constant retention of sulphur and magnesium. These findings agree with the known processes going on in the bones. On the one hand, the abnormal excretion of calcium is the result of the decalcification and absorption of old bone (*halisteresis*), and on the other, the retention of sulphur and magnesium results from the formation of new osteoid tissue which McCrudden has found to be rich in these two elements and poor in lime salts. In other words, the bones in osteomalacia are poor in mineral matter and especially lime, while relatively rich in organic constituents. It has been shown that the bones of normal women during pregnancy may show a moderately deficient content of lime, a so-called "physiologic osteomalacia." Obviously during the development of the fetus there is a greatly increased demand for calcium which is probably met very largely at the expense of the maternal bones. It is McCrudden's conception that the osseous system ordinarily acts as a storehouse of lime. With a single pregnancy the drain on the mother's bones for lime is probably insufficient to produce symptoms, and if a second pregnancy does not immediately follow the deficiency in lime is soon made up. If, however, several pregnancies follow at short intervals the system is unable to maintain a lime balance. McCrudden says, "In other words, it is only after a long-continued and severe drain on the bones of a poorly nourished patient that the body fails to respond to the demands on it, and even then recovery follows if the severe demands are not continued. . . . After repeated, rapidly following pregnancies the amount of calcium phosphates in the bones becomes less and less. A new pregnancy begins before the organism has made up for the loss of calcium phosphate in the preceding pregnancy. The condition of greatest importance would seem to be a marked

tendency to overprolongation of the period of calcium flux." Such a theory is entirely in keeping with Cohnheim's conception of bone as a living tissue, which in keeping with all other living tissue is constantly undergoing changes due to both anabolism and catabolism. In osteomalacia the normal metabolic balance is upset. The reason for this disturbance of bone metabolism in the puerperal form, as interpreted by McCrudden, seems a satisfactory one, but in the case of the non-puerperal osteomalacia the cause is not evident. In general, it would appear that a great variety of causes, such as infections, endocrine disturbances, undernutrition, and unhygienic life, may very well be responsible for the disturbance in the calcium metabolism.

**Clinical Features.**—The onset of the disease is so insidious and irregular that it is seldom recognized until the skeletal alterations have reached an advanced stage. The clinical picture is then quite constant and distinctive. In the earlier stages before the objective signs are well developed, the condition is often diagnosed as "rheumatism."

The most prominent and constant subjective symptom is pain, which may be of almost any type and severity. It is characteristically of a very severe, dull nature, felt over the affected bones and increased by walking as well as pressure over the affected parts. The intensity is frequently worse at night. Intense crises of pain may occur. A considerable variety of symptoms referable to the muscles usually accompany the pain. Weakness and stiffness are almost invariably present. Cramps, tremor, spasms, and contractures are common. Fatty degeneration of the muscles amounting to almost complete lipomatosis has been described. The muscles of the leg, especially the adductors of the thigh and flexors of the knee, are held rigidly to prevent motion. Because of the pain with motion the patient is apt to resist any manipulation. I have already demonstrated all of these features in the case before us.

Walking becomes difficult and the gait is of a very peculiar spastic, waddling type, commonly designated as the "duck gait." When standing or walking the patient has a tendency to lean forward. Exaggeration of the deep reflexes, paresthesias,

and a considerable variety of psychic disturbances are often seen.

One of the outstanding features of the disease is the multiple spontaneous fractures which are mostly confined to the ribs and the long bones of the extremities. They are invariably transverse and seldom complete. The fractures are not usually due to an actual break following bending, but should be interpreted as a giving away or crumpling of the disintegrating bone. Only an insignificant callus is formed. Dislocation of the bone does not result, though deformities are the rule. When the fractures have been very numerous the resulting distortions may take on the most extraordinary forms.

In consequence of the fractures, bending and crumpling of the bones, the outward deformities are extreme, and because of the variation in the distribution and extent of these changes without uniformity. The height is diminished. All degrees of lordosis, kyphosis, and scoliosis develop, with resulting deformity of the thorax. Most constantly of all, in the puerperal form, are the changes in the form of the pelvis. It is compressed both downward and laterally. In the legs the deformity takes the form of a broad irregular more or less forward curve.

With the progression of the fractures and contractures the patient gradually becomes bedridden. Ankylosis and distortion of the joints soon follow. Finally, a stage of utter helplessness is reached, and the way is open for all sorts of complications and functional disturbances.

In puerperal osteomalacia menstruation is usually normal, and it is generally stated that women suffering from the disease are unusually fertile. Parturition during the early stage of the disease is normal, but in more advanced cases, because of the pelvic deformity, delivery is impossible except by cesarean section.

The blood shows no constant abnormalities. Anemia may be present and hyperleukocytosis, with increase in the number of myelocytes and eosinophils, has been reported. The calcium content of the blood is said to be increased. The amount of calcium and phosphate in the urine is so variable that no diag-

nostic or prognostic significance can be attached to such determinations.

**x-Ray Examinations.**—*x*-Ray studies of the skeleton should always be made in all suspected cases. The roentgenographic appearances are distinctive long before the deformities are sufficiently characteristic to warrant a diagnosis. In all affected bones, but especially in the long ones, the most striking change is the broad or angular curves and irregular outline. Multiple incomplete fractures with little or no callus formation is also a prominent feature of the *x*-ray picture. As to the structure of the bone, the main changes are as follows: (1) dilatation of the medullary canal, (2) thinning of the cortex, (3) general and extreme rarefaction of the osseous tissue, which appears indistinct, without trabeculation, and shows hardly any contrast with the soft parts, (4) epiphyses very thin, but usually without deformity.

The course of the disease is almost invariably chronic, although in a few instances it has been known to progress to a fatal termination in a few months. The usual duration is measured in years. Scott<sup>1</sup> gives statistics of a series of cases the average duration being six and a half years and the maximum thirty years. In the puerperal form the chief factor influencing the course is the number of pregnancies. The disease appears at times to become quiescent. The general death-rate in osteomalacia has been variously estimated as from 70 to 85 per cent.

**Treatment.**—Early diagnosis is of the utmost importance, since favorable results from therapeutic measures are in inverse ratio to the stage of the disease when begun. If an arrest of the process in the bones takes place in the early stages the permanent deformity is relatively slight. Excellent results following treatment have occasionally been reported, but in general much less brilliant than those recorded in many cases of the so-called "hunger osteomalacia." The greatest care should be exercised to prevent fractures, as by the choice of a suitable bed and mechanical support when the disease is advanced and the bones

<sup>1</sup> Indian Jour. Med. Res., Calcutta, 1916-17, iv, 140.

very weak. Surgical treatment has no place in the program of treatment.

Since osteomalacia is so definitely associated with bad hygiene and undernutrition, attention to all the details of the patient's life and environment is indicated. Rest, fresh air, and hydrotherapy are the first essentials. A liberal varied diet containing a high percentage of albumin, lime, and phosphorus should be provided. Of the simple foods containing these elements may be mentioned meat, fish, eggs, milk, and green vegetables. Remarkable response to the feeding of large amounts of fat have been claimed in "hunger osteomalacia." The most prompt therapeutic effects of the fats are said to follow the use of those of animal origin, namely, butter, beef fat, mutton fat, and especially cod-liver oil. This response to fats is attributed to the "fat-soluble A vitamin" contained in the fats just mentioned. The vitamin content of cod-liver oil is much in excess of that of any other animal fat, and this presumably bears some significant relation to the fact that this preparation appears to produce greater effects than the others.

Gestation and nursing should be avoided. There can be no question of the improvement in many cases following oöphorectomy, but, as I have already stated, the evidence is that this is due not to any influence on the bone metabolism, but simply to the prevention of gestation. The only justification for castration would therefore seem to be in those cases where gestation cannot be prevented by some other measures. Sterilization can be produced much more simply by the use of the *x*-rays.

Drugs are of questionable value. A wide difference of opinion exists as to the value of adrenalin subcutaneously. By many it is advised as the sovereign remedy, while a greater number of clinicians condemn it as without merit. It is said to give great relief from pain (1 c.c. of a 1 : 1000 solution every second day). The classical remedy is a phosphoric acid and cod-liver oil mixture (.01 per cent. phosphorated cod-liver oil), 2 to 4 teaspoonsful daily, and increased gradually. It certainly merits a thorough trial. Calcium lactate or carbonate are advocated by many, but their value has not been established.

CLINIC OF DR. WILLIAM H. ROBEY

BOSTON CITY HOSPITAL

**TWO CASES OF CARCINOMA OF THE ABDOMEN IN  
YOUNG MEN—ONE TWENTY-EIGHT AND THE  
OTHER THIRTY YEARS OLD**

THE chief interest is in the youth of the patients and the difficulties of diagnosis.

**CARCINOMA OF THE STOMACH**

A Russian, twenty-eight years old, single, entered the hospital on February 2d with a complaint of pain in the stomach. He was referred from the O. P. D. because of a mass in the epigastrium. He had had indefinite pain in the epigastrium for six months. He did not vomit and there was no periodicity of pain. He did not think there had been any loss of weight, but because of weakness and the epigastric pain he had given up work two weeks before. He stated that six months before he had had a slight attack of abdominal pain, consulted a physician, and was relieved. He was comparatively comfortable until two months ago, when he was seized with a sudden sharp pain in his left side while carrying a heavy box. He dropped the box, the pain soon passed off, but came on at irregular intervals of a week or ten days. There was a sensation of needles sticking into the epigastrium, sharply localized, and, although always present, it was more severe after eating. He raised small amounts of gas, but did not vomit. No distended feeling and no sour regurgitation. The bowels were very constipated and moved only with oil or enemata. He was unable to sleep because of the pain.

**Present History.**—He had not had the diseases of childhood. He had pneumonia three years before, but no other acute illnesses. During the last two weeks there had been frequent

headaches, but never before. No cardiac nor respiratory symptoms. No history of venereal disease. Negative renal history except for nocturia two or three times for several years. Previous to the present illness there had been no indigestion. The bowels were regular until two weeks before.

**Family History.**—Entirely negative. No history of tuberculosis, cancer, or insanity.

**Physical Examination.**—Upon entrance to the hospital the patient was considered well developed, but poorly nourished. The head, eyes, mouth, throat, and neck were normal. The teeth were fairly good and the tongue clean. The thorax was well developed, symmetrical, with regular, even respirations, and good expansion. The lungs were negative. The heart action was regular and strong, without evident enlargement. A soft systolic murmur, not transmitted, was heard. The pulse was strong; arteries slightly sclerosed and easily palpable. In the abdomen a firm, round, smooth mass was felt just below the costal margin to the left of the median line, which, on being palpated, seemed to disappear, but was brought out after the patient sat up and then lay down again. It was slightly tender, although it could be moved about from side to side with freedom. This ease of motion suggested the possibility of a bellying of the abdominal wall or of some omental tumor before its real nature was determined. It seemed too superficial to be in the gastro-intestinal tract.

The liver was just palpable below the costal margin. The extremities were without edema and the reflexes equal and normal.

On February 6th gastric analysis showed absence of HCl in both fasting contents and the test-meal.

February 10th the x-ray department reported: "An inter-gastric tumor of the lower third of the stomach. Lower third of the stomach fills irregularly, consistent with malignancy. Remainder of gastro-intestinal tract essentially negative. Slight ptosis of the transverse colon."

The patient looked fairly well, but stated that his symptoms were more marked and the dull pain was constantly present.

February 16th, the patient having been on a meat-free diet, the stool was positive for occult blood. A surgical consultation was held. In view of the rapidly increasing tenderness, absence of free HCl, blood in the stool on meat-free diet, and the *x*-ray report a diagnosis of malignancy was made in spite of the age of the patient, and an exploratory laparotomy advised.

The Wassermann test was negative—the urine not remarkable. The Hg. was 85 per cent. and the white cells on two counts were 10,000. There was a moderate fever ranging between normal in the morning and 100° F. in the evening.

At the surgical examination on February 16th there was found in the epigastrium, just to the left of the midline, a firm, rounded tumor the size of a baseball, not particularly tender, which moved upward and downward freely with respiration. The abdomen was opened by Dr. J. C. Hubbard, who found a firm, irregular tumor involving the lower third of the greater curvature of the stomach, without obstructing the pylorus, but firmly adherent to the transverse colon. Lymph-nodes were enlarged. Two small tumors were found in the liver. A diagnosis of inoperable carcinoma was made and the abdomen closed.

On February 17th the patient appeared to be making post-operative recovery, but on the 18th he looked very sick. The abdomen was soft and not tender, but the temperature had risen from normal to 103° F. and the patient died at night.

**Discussion of the Case.**—At the time of admission to the hospital the patient's youth, negative gastric symptoms, appearance of health, and the freely movable tumor led to a consideration of a number of conditions without particular emphasis on malignancy. The mass seemed too superficial to be in the stomach. At times during palpation it appeared to vary in size. *Echinococcus* cyst was considered. When of moderate size these cysts may exist for some time without producing any symptoms. Osler says that an irregular, painless enlargement, particularly in the left lobe, or the presence of a large, smooth, fluctuating tumor of the epigastric region is also very suggestive, and in this situation, when accessible to palpation, it gives the

sensation of a smooth, elastic growth and possibly the hydatid tremor. Syphilis may produce irregular enlargement without much disturbance of the general health—sometimes also a very definite tumor in the epigastric region—but this is usually firm and not fluctuating. The various forms of tubercular tumors and glands were considered, but the absence of tubercular signs elsewhere and the temperature chart dismissed this possibility. Finally, because of the rapidly increasing tenderness, absence of free HCl, and the x-ray report of a gastric tumor, a diagnosis of malignancy was made notwithstanding the patient's age of twenty-eight years.

#### CARCINOMA OF THE MESENTERIC LYMPH-GLANDS

J. E., a Greek, aged thirty years, single (No. 434,213), entered the Medical Service January 1, 1922, complaining of cough, weakness, night-sweats, and diarrhea. He had had gonorrhea three years before, and again two years later, but at the time he entered the Boston City Hospital there were no venereal symptoms. He had lost weight and strength in the past year, especially in the last six months. There were cough and night-sweats for eight months; the cough at first was dry, but for a while there had been a thin, greenish sputum, especially in the morning, but never any blood. There was headache often in the afternoon and for ten days a diarrhea. He had a fair appetite, no nausea, vomiting, nor jaundice.

The family history was quite negative and the patient gave a past history of only one important disease. He had typhoid at nineteen and was in bed for three months. He used alcohol freely until three years before, but very little since. His weight three years before was 130 pounds and was 125 at entrance. He had lived a very unhygienic life with all forms of excesses except tobacco, from which he had entirely abstained.

**Physical Examination.**—Fairly well-developed, poorly-nourished white man, lying quietly in bed. Mentally clear and active.

*Head.*—Symmetrical. No scars or exostoses.

*Eyes.*—Pupils regular and equal; react to light and distance.

Sclerae clear. No nystagmus, exophthalmos, nor strabismus. No ptoses nor edema.

*Ears*.—No tophi, discharge, nor tenderness.

*Nose*.—No obstruction, external deformity, nor discharge.

*Mouth*.—Teeth all out. Tongue clean and protrudes in mid-line without tremor. Mucous membranes clear.

*Throat*.—Tonsils slightly enlarged. No redness or exudate.

*Neck*.—No glands, thyroid tumor, nor stiffness.

*Chest*.—Symmetric, fair expansion. Supra- and infraclavicular spaces retracted.

*Lungs*.—Normal tactile fremitus. Entire right back is dull, otherwise lungs are resonant. Breathing is regular throughout except over right lung in front, where it is bronchial. No râles heard except a few musical râles over left anterior lung near sternum. No pleural rub.

*Heart*.—Apex-beat diffuse. Seen in the fifth space, nipple line. No thrill palpable; sounds clear and strong except for soft blowing systolic murmur at apex, not transmitted.

*Pulses*.—Regular and equal. Normal volume and tension; wall not palpable.

*Abdomen*.—Somewhat rigid. Tympanitic. Tender over both lower quadrants, more on left. No spasm. Liver not palpable. Spleen and indefinite mass palpable down to umbilicus. Left inguinal hernia.

*Extremities*.—No edema, scars, ulcerations, or tenderness.

*Reflexes*.—Knee-jerks equal and active. No Babinski or ankle-clonus.

*Glands*.—None enlarged.

*Skin*.—Negative.

After the physical examination of the patient we summed up the case as follows:

The present symptoms were consistent with pulmonary tuberculosis, the definite right-sided pleural rub and the dulness at the left base, with decreased voice and breath sounds and a fluid line by x-ray examination, suggesting, along with loss of weight and strength, the above diagnosis. In addition, however, he showed a mass or, rather, two separate masses in the left

upper quadrant. In the first place a mass which felt like a spleen and which came down on inspiration. Between this mass and the midline was a second mass which did not move with inspiration. It was firm and of some irregularity of contour. It extended down as far as the umbilicus, where a rounded edge could be felt having the consistency and contour of the lower pole of the kidney. The kidney may have been pushed down by the mass above. Hypernephroma, sarcoma, and tubercular kidney were considered as possibilities. The mass felt firm and not cystic. The urine examination was negative.

January 25th: The patient coughed very little and the small amount of sputum was negative for tubercle bacilli. A second x-ray examination of the chest failed to show a fluid line, but suggested tuberculosis of the right apex. The left costal margin in the axillary line appeared to bulge outward more than the right.

February 11th: Since the last note the patient continued in about the same condition. There was still some pain in the lower chest. During the interim the chief attention was given to a study of the abdominal mass, which was distinctly increasing in size, and was thought to be either a malignant growth or tuberculosis of the kidney. The final opinion at this time was that the patient had a chronic splenitis, which was independent of the other mass. Upon a superficial examination it might appear that there was but one mass, but on careful examination a sulcus between the two could be definitely made out by the examiner.

March 7th, the patient being in about the same condition, he requested discharge from the hospital, but re-entered on March 15th. His return was due to lessening strength and lack of home care. At the time of his re-entry the physical examination was practically unchanged. The tumor was about the same, causing bulging of the lower ribs and raising the left diaphragm to the fifth rib in the anterior axillary line. It could be grasped by both hands, one placed over the lumbar region and the other over the abdomen, and could be felt to move *in toto* on pushing from one hand to the other. The lateral border of the tumor

was quite smooth and the sulcus already described could be felt. Dr. Larrabee, of the Blood Service, thought that it was not an ordinary case of splenomegaly, but more likely tuberculosis, cancer, or some other disease of the spleen. The blood report showed some anemia, but was otherwise unimportant.

*Report of Examination by the Blood Service*

Blood:	Hgb.....	68 per cent.
	R. B. C.....	3,200,000
	W. B. C.....	6,200
	Platelets.....	114,000
	Retic. R. B. C.....	2.2 per cent.
	Poly. neut.....	71 "
	Eosinophils.....	5.5 "
	Mast cells.....	1 "
	Lymphocytes.....	19 "
	Myelocytes.....	0.5 "
	Smear about normal	

Dr. Shattuck, of the Department of Tropical Diseases, also examined the patient, and was about to perform a puncture of the spleen when an *x*-ray examination by the Genito-urinary Service directed our attention to another factor. Dr. Shattuck considered a probable diagnosis of tubercular peritonitis, and doubted a tumor of the spleen or kidney. The examination for ova and parasites was negative. A barium enema showed a negative large bowel with displacement deformity. It was our opinion that a localized peritonitis was hardly possible because with such marked involvement there would be other signs, such as fluid, distention, and intestinal disorder.

April 2d: A pyelogram was successfully made, with the following report: The left kidney was high with tortuous ureter. Dr. Howard found both kidneys enlarged, with the pelvis of the left very much more so. The ureter was kinked. A catheter on the left passed about one-third of the way up the ureter, when a resistance was met. A pyelogram of the right kidney gave a normal appearance. Catheterized specimens from the left contained the *Staphylococcus aureus*, while the right kidney was sterile. On inflating the peritoneum with

oxygen over the left kidney region an oval mass 10 to 15 cm. in diameter corresponding to the left kidney was made out. The spleen could be seen separately as an elongated mass about three times its normal size, lying along the ribs and extending between them. In view of this examination a diagnosis of primary tumor of the kidney was made, with an enlarged and congested spleen.

April 7th the patient was transferred to the Genito-urinary Service for operation. At operation by Dr. Howard the left kidney was found to be slightly enlarged, normal in color, with a large dilated pelvis pushed to the extreme left. The spleen projected downward, was enlarged to twice its normal size, and pale in color. Above the left kidney was a large rounded, irregular mass which ran from the top pole of the kidney to the diaphragm. The kidney and the tumor appeared to be one continuous mass. The attempt at removal was difficult because of firm adhesions. The left kidney was finally dissected from its capsule and removed. After the kidney was removed the mass was more accessible, was freed from its adhesions, tied off, and removed. It looked not unlike a cauliflower. Considerable shock resulted from the operation and, notwithstanding vigorous stimulation, the patient died three hours later.

*Autopsy Report (May 1, 1922)*

Autopsy twenty-one days postmortem.

Body length, 175 cm. Age thirty years.

Clinical diagnosis: Tumor of the kidney. The body is that of an emaciated, poorly developed, adult male. Lividity of dependent parts. No edema. Pupils 4 mm. in diameter. Several scratch-marks present over the chest and abdomen. There is a transverse incision across the recti and oblique muscles 15 cm. long, about midway between the lower edge of the ribs and the crest of the ileum, closed by silkworm sutures. The incision is recent and shows no evidence of infection.

*Peritoneal Cavity.*—The incision mentioned above opens into a pocket from which the left kidney has been removed. The tissue about this space is blood tinged; evidence of recent opera-

tion, but no evidence of hemorrhage. Two mesenteric lymph-nodes located just below the pancreas are enlarged and hard, measuring 4 by 2 and 5 by 3 cm. When sectioned they consist of hard, white granular tissue with a dark brown, hematogenous center, apparently necrotic, about which is a delicate bluish colored line of demarcation. Appendix negative.

*Pleural Cavity*.—Negative.

*Pericardial Cavity*.—Negative.

*Heart*.—Weight 300 gm. The muscle has a bluish tint, probably postmortem; is firm. Valves negative.

Measurements: Tricuspid valve, 10.5 cm.; pulmonic valve, 5.5 cm.; mitral valve, 10 cm.; aortic valve, 6.5 cm.; left ventricle, 1.5 cm.; right ventricle, 0.4 cm.

*Lungs*.—In the posterior edge of the right lower lobe are several small round, hard foci, which, sectioned, are firm, white, and granular, about 0.7 cm. in diameter. All are about the same size. One similar nodule of about the same size is present in the edge of the left lower lobe also. Otherwise the lungs are negative.

*Spleen*.—Weight 325 gm. Is enlarged about four times normal size. Capsule negative. Pulp solid, not scraping away. Trabeculae are visible, but follicles not seen.

*Gastro-intestinal Tract*.—Negative throughout.

*Pancreas*.—Soft, showing evidence of postmortem changes.

*Liver*.—Weight 2070 gm. Is somewhat enlarged. Scattered throughout the organ are many fairly rounded, white, hard foci, which, when sectioned, are composed of white, hard granular tissue ranging in size from a few millimeters to a little over 2 cm. in diameter. The liver lobules are indistinct.

*Kidney*.—Left has been removed. Right, weight 140 gm. Markings are distinct. The capsule strips easily from the smooth surface. Cortex thickened, being 0.7 cm.

*Adrenal*.—Right seems small and thin.

*Bladder*.—Negative.

*Genital Organs*.—The prostate is somewhat enlarged, but shows no evidence of tumor or infection.

*Anatomic Diagnosis*.—Metastatic tumor (carcinoma) of

mesenteric lymph-nodes, liver, and lungs. Recent abdominal incision and removal of the left kidney. Scratch-marks over chest and upper abdomen.

**Differential Diagnosis.**—As already indicated, that all of us were considerably puzzled cannot be denied. Malignancy of the kidney was the most prominent diagnosis, with possible secondary involvement of the thorax. There was no question in our minds previous to operation that there were distinct enlargements of the left kidney and spleen. Even after the  $x$ -ray examination that we were dealing with a primary growth of the kidney was shown by its enlargement and kinked and obstructed ureter. The mass about the left kidney did not appear in any form of examination, and the interesting part is that if we had to deal with a similar case, could we come any nearer to the correct diagnosis than we did in this one? It is my belief that even with this case in mind one might make the same mistake a second time. You will see that the kidney was pressed upon and distorted by a nearby growth which did not show itself in any way.

These 2 cases show the importance of considering the possibility of carcinoma even in quite young people. Tuberculosis of the peritoneal cavity would hardly show such a dense mass without other physical signs. Twelve sputum examinations were made for tubercle bacilli, and all were negative. The Wassermann was negative and also the several urinary examinations.

CLINIC OF DR. GEORGE R. MINOT

MASSACHUSETTS GENERAL HOSPITAL

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### THE RÔLE OF A LOW CARBOHYDRATE DIET IN THE TREATMENT OF MIGRAINE AND HEADACHE

"HEADACHE," said Cullen, "as a disease, it is obscure, as a symptom, difficult." This is certainly as true today as two centuries ago. The diagnosis and treatment of disease in individuals with headache as the principal symptom particularly require the art of medicine; an art which can never be practised by positive rules, or perhaps carried to absolute perfection. This art cannot be practised without an acquaintance with various sciences, the principles of which are to be consulted daily in the exercise of it. Even so, science has as yet yielded comparatively little information regarding the etiology and the pathologic physiology of the various forms of headache. It is a difficult problem to unravel the cause of headache. Each patient with this symptom must be studied critically and by all the means at one's disposal. Too often one finds that this has not been done. It is exceedingly common to find that individuals who are chronic sufferers from headache have received for treatment but many forms of drugs. This has led them to take an excess of a supposed remedy, which results in more damage than good.

*Headache has no individual entity as a disease, but as a symptom headache may persist a long time as the sole or most prominent complaint the patient has. It may occur from many causes and in practically all known diseases. Headache may arise from organic brain disease, nephritis, cardiovascular abnormalities, anemia, and disturbances attributed to the glands of internal secretion; also during acute and chronic infections.* It

may result from poisons, such as alcohol, lead, and various industrial poisons, as well as from excessive use of tobacco, tea, and coffee. Toxic headaches may arise from other causes, as occurs in such a disease as eclampsia. The eyes may be the cause of a headache from errors of refraction, especially astigmatism and hypermetropia; occasionally they result from defects of the eye muscles. The acute diseases of the eye may also be a source of headache. Inflammatory conditions of the accessory sinuses, nasal disease, and dental defects may be responsible for pain about the eyes and of the head.

*Other causes and forms of headache are more common.* It is in the diagnosis and treatment of patients with these other forms that the art of medicine is so important and where the etiology is much less often obtained and understood than in many of those conditions first mentioned. A complete understanding of the life and environment of these individuals is fundamental. Among these other forms of headache are those of the disease migraine, and those due to improper hygiene and alterations in the habit of the body and mind, as well as due to local conditions of indefinite character.

Numerous theories as to the cause of *typical migraine* have been advanced, yet but little is known about this disease. It is recognized that heredity and predisposition play an important rôle. The disease appears to follow the mendelian law. The symptom complex is characterized by severe paroxysmal headache, typically unilateral, associated with disorders of vision, mental depression, and often digestive symptoms. The mechanism and exciting causes of the attacks are not well understood. Headache alone may be the only symptom, and the disease not infrequently occurs with bilateral rather than with the typical unilateral pain. Prodromata particularly associated with vision are not infrequent. The pain is boring or gnawing, and at times described as expansile. It may be trifling or cause the patient to suffer unbearable agony. Excellent detailed descriptions of the symptoms of migraine will be found in your text-books, so that no further discussion of them will be given here.

The very common forms of *headache associated with functional alterations* of the body may be mild or severe, and occur generalized as well as localized. Their character may vary from being slight and transient to being persistent and intense. Functional abnormalities also appear to cause individuals to suffer more or less definite paroxysms of mild or severe pain in the head. The term *atypical migraine* is applied to many of these cases. Fatigue, emotional and psychoneurotic states, as well as lack of exercise may be the cause of these forms of headaches just mentioned. Many of these patients are poorly nourished, while others are obese. Faulty bodily mechanics are often evident, as are such disorders as those attributed to the female pelvic organs. Improper food and indigestion, particularly intestinal, may contribute to the production of headache and at times be the sole cause. Constipation with its accompanying disturbances may play a rôle, and this I shall refer to later. The multiple conditions that may occur referable to environment, food, and the patient's life often render diagnosis and treatment difficult.

I particularly wish to point out that *among cases of typical and atypical migraine*, both with and without gastro-intestinal symptoms, there are *some* which are distinctly *benefited by diet*. Not only may some cases with recurring attacks of headache be alleviated by suitable food, but also some of those with mild transient and others with more or less persistent diffuse headache. Before considering that digestive disorders or diet are important factors in a given case one must with care eliminate other factors. In some cases the type of food would appear to be the sole cause, while in others it seems but contributory to the production of the symptom, together with such disturbances as instability of the menstrual period, nervous strain, and various psychic phenomena. In any given case the question arises as to whether digestive disorders are the cause or the effect of the diseased state producing headache. Intestinal indigestion is a condition that may be the cause of headache, more usually of a dull, indefinite character, but occasionally may produce recurring attacks. On the contrary, the gastro-intestinal symp-

toms that develop toward the end of a true migraine paroxysm may be looked upon as a result of the diseased state.

It is to be recognized that patients with *intestinal indigestion* may suffer not only mildly and severely from intestinal symptoms but also, without relation to their intensity, experience other manifestations of their disorder. These other symptoms, noted below, may be even more prominent than the gastrointestinal ones. The patient may become abnormally tired and irritable, experience inability to think clearly, and lack initiative. Vasomotor disturbances are frequent. Pruritus, cutaneous eruptions, and renal irritation may be symptoms. Ill-defined pains in different parts of the body occur; and headache, too, in various forms may be a distinct feature of patients with this type of indigestion. The *stool examination*, so often neglected yet of the simplest sort, gives information of value regarding intestinal digestion. Much may be learned from noting the gross character of the feces. One usually finds that carbohydrate rather than protein is contributory to the cause of an intestinal indigestion. In such instances the patient will pass stools that are typically soft and mushy, often foul, with a strong acid odor and reaction. Excess of gas formation is a feature. The stools on passage may show many bubbles of gas, while on standing a few hours many more will form. Such stools when stirred with a stick will crackle. A normal stool will form very few gas bubbles, and often none, even when it has stood twenty-four hours. One may determine the exact amount of gas formed by special procedures, but the simple inspection of the feces contributes the essential information. When protein is intimately associated with an intestinal indigestion the stools are putrefactive rather than fermentative, and are alkaline and often exceedingly foul. Many patients suffering from carbohydrate intestinal indigestion, with or without headache, may be cured by limiting the carbohydrate intake and avoiding the more easily fermentable types, such as ordinary breads and gross sweets. The twice-baked breads, as zwieback and Swedish bread, and dextrinized foods, are tolerated in this condition much better than the more usual forms of bread.

There are *other individuals benefited by limitation of carbohydrate who suffer from headache* which may be a manifestation of typical or atypical migraine, and who do not have symptoms or stools of a type associated with carbohydrate intestinal indigestion. Some of these patients will be found to be taking an excessive amount of carbohydrate, while others are not doing so. It thus seems that the headaches in such individuals may be associated not only with an actual excessive intake of carbohydrate but also with an excessive amount so far as the individual ability of the organism is concerned. This would suggest that there was some congenital or acquired defect in the carbohydrate metabolism of such patients.

Headaches may be associated also with the intake of other foods than carbohydrate, but it appears that starches and sugars play the largest rôle in headaches associated with dietetic error. This has been well emphasized to the profession by T. R. Brown<sup>1</sup> and others.

The intake of *animal protein food* may be intimately *associated with headache*. When such is the case, it is rare to find that the intake of a special animal proteid is related to the symptom. However, in a few cases headache occurs following a special food, and this has suggested that the attack is related to a specific sensitization. Even so, protein skin sensitization tests are usually negative. An occasional case may be explained, however, by obtaining a positive skin reaction to some food substance, as egg. In such cases such symptoms as arthralgia, erythema, urticaria, and edema are apt to be present. In a few cases, usually with symptoms suggesting gout, the purin elements of the diet appear to play a rôle in the production of headache.

Before commenting further on the improvement of headache by reduction of carbohydrate I wish you to remember that many *patients with altered gastro-intestinal function* from many causes *may experience some form of headache*. If they do so their headaches often are benefited or disappear with improvement or cure of the gastro-intestinal condition, which is usually

<sup>1</sup> Jour. Amer. Med. Assoc., 77, 1396, 1921.

brought about through a change in the program of life and by the taking of suitable food in an adequate manner.

Individuals who suffer from *constipation* may have headaches. This condition alone undoubtedly produces a variety of types of pain in the head. It probably usually does so by means of the accompanying disturbance of intestinal carbohydrate fermentation or putrefaction of protein, even though stool examination may not yield definite evidence of such alterations. A reflex from distention of the colon may be the cause in some instances. The abuse of laxatives may permit irritation of the bowels and thus intensify headache. Many patients with dull, not recurrent attacks of headache, who are constantly irritating their intestines with drugs will suffer no longer from head pain if laxatives are withdrawn. To do so may be difficult for the patient, but perseverance with approved methods for regulating the bowels will result in cure and great happiness to many persons.

Food is directly or indirectly associated with headaches of various types occurring with altered gastro-intestinal function. I wish to emphasize to you that there occurs a group of patients with periodic headaches and some with chronic persistent headache in which gastro-intestinal symptoms may be absent, slight, or marked, who are benefited by reduction particularly of carbohydrate and occasionally of protein. *One may suspect, but never perhaps be able to foretell definitely whether a patient with headache of the migraine type, typical or atypical, or with diffuse chronic headache will be relieved by reduction of carbohydrate.* Quite often the patient will recall that paroxysms follow the excessive intake of candy or other form of carbohydrate. In other cases one learns from the individual nothing to suggest a relationship of his symptoms to his food. In some such cases an analysis of what the patient is accustomed to eat will reveal that he takes excessively of carbohydrate; either an absolute excess or a proportionate excess to the other kinds of food. Others give no evidence of having partaken of an abnormal diet. If the stools are of a type associated with carbohydrate indigestion, it is significant that benefit will occur with a proper

diet. However, the majority of the cases that improve after reduction of carbohydrate show no abnormality in the stools.

There have been no complete studies on the *metabolism of these patients*. The fasting blood-sugar is often normal; a rare case may give an elevated figure. The determination of the blood-sugar two hours after the ingestion of 1.5 grams of glucose per kilogram of body weight has shown that it is often normal. In some cases, however, the blood-sugar returns to normal distinctly slowly, and sometimes not for six hours, though it does not reach very high figures. When such is the case it appears that decrease of carbohydrate will usually be beneficial. Such, however, is not always so, for I have observed patients with severe migraine who have responded abnormally to the sugar tolerance test without the slightest benefit having resulted from dietary measures. *The ultimate criterion to decide whether carbohydrate is associated with the production of headache rests with the therapeutic effect of diet*, properly administered, and likewise with the production of the symptom following the intake of an known excessive amount of carbohydrate. It is to be clearly recognized that though many cases can be alleviated by dietary measures, there are *many others that derive no benefit from diet*.

The term *bilious or sick headache* has often been applied to some of these cases with migraine and atypical migraine when gastro-intestinal disturbances, especially vomiting, have been associated with the attacks. In such cases purgation or starvation often abort attacks or bring relief of symptoms. *Alteration in liver function* appears to occur in some of these patients, so that the term "bilious" is not so inappropriate as some are led to believe. A distinct increase in the size of the liver may occur during an attack. This is demonstrated by the organ becoming palpable and sometimes tender, decreasing so it cannot be felt between the paroxysms. Further evidence of altered liver function is shown by the fact that we have observed that there occurs, at least in some cases, a definite abnormal amount of bile-pigments in the plasma coincident with the headaches. In such patients the bile-pigments in the plasma

have been normal between attacks. The urine very rarely shows bile, though the patients may look pale and slightly sallow following an attack. Slight jaundice of the sclerae rarely occurs, as does an acholic stool. There are groups of cases recorded where the development of definite liver disease has occurred in sufferers from migraine. For instance, cases of xanthoma often have migraine as well as prolonged jaundice. A careful study of the bile-pigment output and liver function would be of interest in patients with atypical and typical migraine. A few observations suggest that with the attack there is a decrease in the bile-pigment output followed by an increased output quite likely dependent upon an active congestion of the liver. This is probably a result of altered gastro-intestinal function or digestion.

*I will now show you a patient with typical migraine who has been distinctly benefited by a low carbohydrate diet.*

*The patient* is a woman thirty-five years of age, a school-teacher by occupation. Three months ago she first sought relief at this hospital for her periodic headaches. *At that time she gave the following history:*

Ever since the age of fourteen she has suffered at intervals of from one to six weeks from attacks of severe headache especially confined to the right side. The attacks have become more frequent and of longer duration in the past four years, but their character has not changed. Approximately, every sixth attack is much more severe than the others, while only a few have been distinctly mild.

The day before an attack she has often felt unduly irritable, fatigued, and experienced unfounded anxiety. It is to be noted that such symptoms frequently precede the headache in many cases of migraine.

This patient's pain nearly always commences after breakfast, beginning about the right eye, especially above it. It then soon becomes boring, radiating internally to the eyeball, and particularly "in a straight line through the skull to the back of the neck." The intensity of the pain continues to increase for several hours, and usually develops to such severity

that she is unable to pursue any duties or pleasures. After six to eight hours the pain lessens, but some discomfort is present for from twenty-four hours to three days. Motion of the head or eyes aggravates the pain, while bright light and noises create a sensation of pain. Occasionally she has noticed a darkening of the visual field during the early part of an attack. At the onset of an attack there has occurred rarely the sensation of seeing dazzling colored lights before her eyes. The pain has at times been confined to the left side, and if so it has been less intense than when on the right. Sometimes the pain becomes generalized and of a dull expansible character. There has been no unilateral paresthesia, transitory aphasia, or periodic oculomotor paralysis as occurs in some cases of migraine.

In the past four years nausea followed by vomiting has occurred with most attacks. It usually commences as the intensity of the headache begins to decrease. Vomiting is then apt to recur intermittently for some hours, or even for two days. It is associated with distention of the abdomen, loss of appetite, and lameness in the epigastrium. Between attacks she has had no gastro-intestinal symptoms except as noted below. For four years she has suffered for frequent periods of days from some belching of gas after eating, and occasionally has been bothered by a mild sense of pressure on the right side of her abdomen. On account of these symptoms her appendix was removed three years ago. She was told that it was "essentially normal." Since its removal she has had no discomfort on the right side of her abdomen, but has continued to raise gas after food. In the past three years she has tended to be constipated and is apt to be nauseated in the morning, so that she has little desire for breakfast. Licorice powder has been taken every other night for two years because she was advised "to be sure to keep her bowels flushed." She is inclined to believe that she feels less nauseated and raises less gas on the days following the evenings when she does not take the licorice. Even so, she has taken this drug because she was told it was most important to do so. She gives no history of passing an abnormal amount

of gas by rectum, as is usually the case in individuals with typical intestinal indigestion.

Following an attack of headache she appears pale and is said to look slightly sallow. The patient was observed by us in an attack that occurred the day after she was first seen. During this paroxysm of headache the liver became palpable. It has not been felt between attacks. Her blood-serum between attacks has shown on several occasions no abnormal amount of bile-pigment, but at the time of the paroxysm of headache it showed a definite increase above normal of the bile-pigment content. Coincident with the attack the patient was not jaundiced, nor did the urine contain bile.

For the past two years she has had no catamenia. For several years, beginning ten years ago, she had a profuse amount of menstrual flow. Curettage was then performed, following which the periods were regular and normal until they ceased two years ago.

In spite of the fact that she has seen numerous physicians, it is noteworthy that none has ever given her any advice about diet. She has, however, received many prescriptions for drugs for the relief of headache and constipation. Likewise, numerous prescriptions for different kinds of eye-glasses have been given her. She herself is inclined to believe that her headaches are associated with food. The patient volunteers the information that it is her custom to partake of sugar very generously. She frequently eats much candy and believes that it may precipitate a headache. She says, "I am rather loath to admit this, as I hate the idea of giving up candy, but believe it would aid to decrease headaches if I did so." Further inquiry regarding her diet informs us that it has been her habit to take practically only carbohydrate for breakfast, usually seven slices of bread a day, and vegetables, fruits, and protein food distinctly sparingly.

Her work is not unusual or trying. She has plenty of time for rest and recreation, but obtains little exercise. She seldom walks over three-quarters of a mile in a day except in the summer.

In the past she has had no diseases other than those mentioned except scarlet fever and measles as a child.

Her *family history* is of importance because it indicates that she has inherited the disease migraine, or a predisposition to it. Her mother and maternal grandmother both suffered from headaches of the same type as hers, while her older sister has the same condition. Her sister's headaches have greatly diminished in frequency and intensity in the past two years, coincident with her menopause. The cessation of migraine paroxysms at this time in life is of frequent occurrence. It is well to recognize this when treatment is given at the time of the menopause, so that one will not unjustly attribute improvement to the form of therapy instituted.

Other members of this patient's family have had neither migraine, arthritis, gout, asthma, or other chronic diseases. Two sisters are living and well. Her father died from a gunshot wound. He had no brothers or sisters. Her mother's only brother and sister are healthy.

*Physical Examination.*—The patient stands 5 feet, 7 inches and weighs 158 pounds. She is slightly obese. Her posture is poor, with rounded shoulders and a prominent abdomen. The complete physical examination reveals no further significant abnormalities. The eye-grounds are normal; she has slight astigmatism. There is no elevation of blood-pressure. The systolic pressure is 120, the diastolic 85. There are no signs of endocrine disturbance, and her basal metabolic rate is +5 per cent.

The *laboratory examinations* show the following:

The *stools* are formed, of normal color and consistency, but somewhat loose after taking licorice. It is slightly alkaline. There is no excess of gas formation. Microscopically nothing abnormal is noted.

The *urine* is negative in all respects.

The *hemoglobin*, *red cells*, *white cells*, and *platelets* are normal.

The *Wassermann reaction* on her blood-serum is negative.

The *fasting blood-sugar* is 0.09 per cent. The blood-sugar was normal and no sugar appeared in the urine two hours after

the ingestion of 1.5 grams of glucose per kilogram of body weight.

At the time the patient was first seen information was obtained regarding her diet that suggested that a decrease in her carbohydrate intake would be advantageous. Shortly after her first visit she was given instructions regarding diet, which she has followed to date. Briefly, her diet has consisted of about 2200 calories, largely composed of proteins, fats, vegetables containing 5 per cent. carbohydrate, and some with 10 per cent., as well as citrous fruits. All forms of sugar and starch except as occurring in the above foods has been excluded. She has thus received a diet adequate for many cases of diabetes.

*Further treatment* has consisted in attention to her constipation and muscular activity. The licorice powder was discontinued, and she has taken a tablespoonful of mineral oil each night. The result has been that she has had a normal bowel movement daily, the change in diet alone probably aiding the formation of a normal stool. Very shortly after stopping her cathartic medicine and beginning the diet her morning nausea, belching, and abdominal discomfort ceased. She has increased her exercise and is walking at least two miles a day, and she has taken suitable exercises to improve her posture.

An adequate amount of *exercise*, and out-door air, without other treatment, often benefits people suffering from headaches, particularly when of a mild generalized type. Individuals will often state that they have fewer headaches in the summer than the winter. They are inclined to believe that the difference is due to the weather. On the contrary, the improvement is not so much due to the weather as to the fact that they obtain more exercise and out-door air in the warmer months than in the colder ones.

It is interesting to speculate on the relation of this patient's altered ovarian function to her headaches. Suffice it to say that altered ovarian function often occurs in cases like hers, and as it returns to normal headaches may decrease, while improvement of head symptoms may be followed by more normal ovarian function. Ovarian preparations may be beneficial for

these patients. This woman has not taken any ovarian extract, and last week menstruation occurred for a day and a half.

Since following for the past three months the régime outlined above this woman has had one mild right-sided headache without gastro-intestinal symptoms. This is in distinct contrast to the severe ones experienced several times in every period of three months in the past years.

The question now arises as to *with what sort of diet the patient should continue*. It is desirable to add carbohydrate to the food intake, anticipating that she will tolerate more. Experience has shown that following a period of sharp reduction of carbohydrate these patients usually can partake of a diet with a greater amount of carbohydrate without precipitating headache. Some can take more than others, while a few must remain on a sharply reduced carbohydrate diet in order to keep headaches at a minimum. The principle to be followed is to determine the maximum amount of starches and sugars that can be taken without the production of symptoms, and to remain on a diet containing just below that amount of carbohydrate. If the patients are overweight a reduction of the total calories is desirable; while if underweight, it is wise to attempt to increase the caloric intake.

This case before you clearly illustrates that there *may be a beneficial effect from a low carbohydrate diet* in typical migraine. It is unreasonable to believe that the other forms of therapy followed out by this patient played more than a small rôle in decreasing her headaches. This is because a reduced carbohydrate diet alone has improved similar cases after no benefit had resulted from suitable treatment for constipation and increase of exercise.

*I want you to clearly understand that unfortunately many cases of migraine are not benefited by this or other forms of diet. Cases of atypical migraine and sufferers from more or less chronic headache are more apt to be benefited by diet than cases of typical migraine. Even so, cases of the former types may not be alleviated by a change in their diet. The mechanism at work*

in the production of the headaches associated with carbohydrate intake is not understood. In some instances alteration in the carbohydrate metabolism may be but a contributory factor, as Pemberton has suggested occurs in chronic arthritis, and in other cases some form of disturbed carbohydrate metabolism may be the primary cause.

There are many aspects of headache and migraine that have been alluded to as well as others not mentioned. It is my intention to simply indicate some features of these cases, and that diet, especially carbohydrate food, may play an important rôle in the production of symptoms in some cases. I also want you to realize that proper treatment for constipation is not by cathartic drugs, and that drugs may lead to worse symptoms than those for which they were prescribed. Each case is a study in itself. Many, unlike the patient I have shown you, lead hurried, complex lives, with mental stress and strain. A simplification of these problems of life forms a fundamental and often difficult task for the physician. Successful treatment demands attention to details. It requires the utilization of all the refinements of medicine, especially the art, but also the science.

CLINIC OF DRS. J. EDWIN WOOD, AND PAUL D.  
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THE INTERPRETATION OF MITRAL DIASTOLIC AND  
AORTIC SYSTOLIC MURMURS\*

THE ability to hear the various heart murmurs and to place them correctly in the cardiac cycle is a great help in the diagnosis of valvular heart disease. Still more important is the interpretation of heart murmurs and their correlation with other physical findings and with the history of the case. Richard Cabot says, "No diagnosis is satisfactory which rests on the evidence of murmurs alone." In spite of frequent warnings like this, some clinicians not infrequently make a diagnosis of valvular heart disease solely on the murmurs heard. This is particularly true if a definite diastolic murmur is present. It will be shown here that even diastolic murmurs may be quite misleading in certain cases. A perusal of the autopsy records of the Massachusetts General Hospital for the past six years has disclosed some interesting errors in the diagnosis of valvular heart disease. The faulty interpretation of certain heart murmurs will be discussed, and suggestions to aid in correct interpretation will be given in this paper along with illustrative case histories and necropsy findings.

The chief topics of interest will be dealt with in this order:

- A. Certain diastolic murmurs heard at the apex of the heart:
  - 1. Diastolic murmurs leading to a diagnosis of mitral stenosis with normal mitral valves at autopsy.
  - 2. Diastolic murmurs almost certainly present, but overlooked, with definite mitral stenosis at autopsy.

\* From the Medical Clinic of the Massachusetts General Hospital.

- B. Certain systolic murmurs at the base of the heart:
  - 1. Systolic murmurs leading to a diagnosis of aortic stenosis, not confirmed at autopsy.
  - 2. Systolic murmurs along with other findings leading to a diagnosis other than aortic stenosis with aortic stenosis at autopsy.

#### A. CERTAIN DIASTOLIC MURMURS HEARD AT THE APEX OF THE HEART

1. **Diastolic Murmurs Leading to a Diagnosis of Mitral Stenosis Without Deformity of Mitral or Aortic Valves at Autopsy.**—For some time it has been observed that a rumbling diastolic murmur at the apex, exclusive of the Austin Flint murmur, is not an infallible sign of mitral stenosis. Fisher<sup>1</sup> was one of the first to call attention to this early in 1894. He says: "Dr. Sansom, in his recent work upon the diseases of the heart, states that the only bruit that can be mistaken for the presystolic bruit indicating mitral stenosis is a diastolic bruit due to aortic regurgitation heard at the apex. There is another sound that at least may lead observers of limited experience to an incorrect conclusion. There is a diastolic or sometimes presystolic sound not infrequently heard at the apex in association with a dilated heart." This author reviewed the records of 13 cases of adherent pericardium (in children) coming to autopsy at Guy's Hospital in seven years. All showed hypertrophy and dilatation of the left ventricle. In the clinical reports of these cases 5 of the 13 presented a diastolic or presystolic bruit at the apex, yet no stenosis was found at necropsy. The author makes this statement about his findings: "It may be said by some that, although there was no actual mitral constriction, the relative size of the mitral orifice was probably small compared with that of the cavity of the ventricle. Whether such is the explanation of the sound or not it does not alter the fact that the bruit did not point to stenosis of the mitral valves."

The following year Phear<sup>2</sup> reported 2 cases observed by him to have apical "diastolic" and "harsh presystolic" murmurs respectively. At autopsy the first showed adhesive pericarditis;

the second had a negative pericardium. Both had marked hypertrophy and dilatation of the left ventricle, and in both cases all valves were negative. He reviewed 46 cases collected from the literature with presystolic or diastolic murmurs clinically and clear mitral valves at autopsy. Aortic regurgitation was present in 17 of these, so that they will not be discussed here. Of the remaining 29 cases, 19 had the apical murmur in question described as "diastolic," "long rumbling diastolic," "middiastolic," or "rumbling diastolic"; the other 10 had it described as "presystolic mitral murmur" or "rumbling presystolic murmur." In all of these 29 cases where observations were recorded there was undoubted and marked cardiac hypertrophy. This author predicates two possibilities in explanation—either shortening and thickening of the chordæ tendineæ or dilatation of the left ventricle.

Osler<sup>3</sup> and Hirschfelder<sup>4</sup> both speak of a certain number of cases of adhesive pericarditis with a rumbling apical murmur heard in diastole. The latter is inclined to explain the presystolic rumble<sup>5</sup> in these cases of adhesive pericarditis (in which aortic, mitral, and tricuspid valves are normal) by the stretching of strands of adhesions with the auricular contraction. Flint<sup>6</sup> says: "A mitral direct murmur may occur in adherent pericardium (chronic fibrous pericarditis) and in large hearts without valvular lesions; in the latter the accessory signs of mitral stenosis are lacking." Cabot<sup>7</sup> finds that Phear's reports of presystolic murmurs in various conditions involving left ventricular hypertrophy accord entirely with his own experience.

In an attempt to arrive at some conclusion concerning apical diastolic murmurs in large hearts, 20 necropsy records of marked cardiac hypertrophy with normal valves were reviewed. The hearts varied in size from 440 to 905 grams (the smaller hearts being relatively quite large in each instance because of the small stature). In each case both the aortic and mitral valves were clear or showed some trifling amount of fibrosis. Four of these had chronic adhesive pericarditis. In no case was there any sign of organic mitral stenosis, the mitral valve circumference varying from  $10\frac{1}{2}$  to 15 cm.

Two of the 20 cases by clinical record had definite and marked mid and late diastolic murmurs at the apex, both leading to false diagnosis. A third had a "probable diastolic rumble" which led to a diagnosis of mitral stenosis. The fourth had a "presystolic murmur" at the apex. These 4 cases were seen by consultants and the murmurs in question confirmed.

An effort was made to find out wherein the large hearts with diastolic murmurs differed from the other hypertrophied hearts of this series. Three of the 4 cases mentioned above with diastolic murmurs had good quality heart sounds clinically, and at necropsy showed "considerable" to "marked" dilatation of the left ventricle. The fourth case with the "presystolic murmur" clinically, did not show left ventricular dilatation postmortem.

Of the 16 cases having no mitral diastolic murmur clinically, 8 presented "slight," "moderate," or "no" dilatation of the left ventricle postmortem. The remaining 8 of this group showed moderate to marked dilatation of the left ventricle, but in every instance but one in the clinical records the heart sounds were characterized as "poor quality," "fair quality," "distant," or "tic-tac." In the remaining case, with an 800-gram heart and marked dilatation of the left ventricle, a review of the clinical record reveals the phrase "no heart sounds audible."

In this series, then, the two factors found necessary to the production of an apical diastolic murmur with normal mitral valves were a vigorous heart action and marked dilatation of the left ventricle. Going one step further the logical explanation of such diastolic murmurs in large hearts seems to be a marked increase in the size of the left ventricular cavity with the normal mitral valve increasing but little in size, thus there being a relative stenosis. Both Fisher and Phear thought this the probable explanation, the latter particularly emphasizing the necessity of the forcible heart action in the production of the murmur. In our series adhesive pericarditis seemed not to be a factor, as it was present in only 1 of the 4 cases with the murmur in question.

Although it is not the purpose of this paper to discuss functional aortic regurgitant murmurs, it is interesting to note that

2 of the 4 cases with mitral diastolic murmurs also had early diastolic murmurs at the base of a high pitch. These were probably not a factor in the production of mitral murmurs in either case, a greater degree of aortic regurgitation being considered necessary in the production of the Austin Flint murmur. Functional aortic regurgitation, while rare, may occur in dilated hearts. Cabot and Locke<sup>8</sup> have reported 3 cases of aortic regurgitant murmurs in severe anemia with normal aortic valves postmortem. Morse<sup>15</sup> has described the functional aortic regurgitant murmur in children with anemia. Recently a case on the wards of the Massachusetts General Hospital with severe pernicious anemia showed a transient early diastolic murmur along the left sternal border. At necropsy the aortic valves were clear.

There is no distinguishing feature of the middiastolic rumble occurring in certain large hearts which separates it from the diastolic rumble of mitral stenosis. The accessory signs of mitral stenosis aid in a diagnosis of that lesion. As mentioned above, Austin Flint says that these accessory signs are absent in large hearts with the functional murmur simulating mitral stenosis. An accentuated pulmonic second sound, a snapping first sound, an electrocardiogram with marked right axis deviation, and sometimes a high P wave would be helpful in diagnosing true stenosis, but not infallible.

Three cases are presented here to illustrate some of the pitfalls already discussed in the diagnosis of mitral stenosis.

**Case I. Chronic Adhesive Pericarditis. Cardiac Hypertrophy and Dilatation. Rheumatic Heart Disease. Mitral Valve Normal.**—L. G. A young white man of thirty-two years entered the Massachusetts General Hospital May 18, 1922 for marked shortness of breath.

**Present illness:** The patient had noticed increasing dyspnea for the past five months. He attributed this to the fact that he had been studying law at a night school in addition to his regular position as an internal revenue agent. One week before entrance he went away for a vacation, but became so dyspneic

that he had to be taken to a small hospital where he received an unknown amount of digitalis and one to two hypodermic injections of morphin every night. After staying there a week he came to this hospital. During the week before entrance here he raised a considerable amount of frothy sputum occasionally blood streaked. He did not notice any swelling of his feet.

*Past history:* He had rheumatic fever at ten years of age and once a year thereafter for five years. Between the ages of fifteen and twenty he was quite active and played ball frequently. After twenty he began to be quite dyspneic on exertion and to have occasional attacks of precordial pain and palpitation. Sore throat occurred frequently, but the tonsils were never removed. No history of venereal disease.

The remainder of the past history was negative except that the patient had been a heavy tobacco user—five to ten cigars daily, one package of pipe tobacco daily, and five to ten cigarettes daily.

*Physical examination:* "A young man propped up on pillows in moderate respiratory distress. Apprehensive expression. Cyanotic ashy color." The tonsils were small, but cryptic. Many fine and moderately coarse râles at the bases of both lungs. Liver enlarged and down to the umbilicus; edge of spleen felt several centimeters below costal margin.

Heart: "Apex impulse very diffuse in third, fourth, fifth, and sixth interspaces. Marked transverse enlargement chiefly to the left; the left border of dulness is in the midaxillary line. Systolic retraction of whole left chest. Broadbent's sign present. Sounds irregular, but slow. Sounds mainly masked by murmurs. A harsh murmur occupies nearly all of systole. A low-pitched diastolic murmur occupies the latter half of diastole. At the base there is a systolic murmur and a loud aortic second sound. A moderately loud diastolic murmur was heard along the left sternal border. Pulmonic second sound accentuated. No thrill felt." The diastolic murmurs mentioned above were confirmed by several clinicians.

The pulse varied from 85 to 110. The blood-pressure was

140 systolic and 70 diastolic. The temperature rose from 99° F. on admission to 101° F. at exitus.

The urine showed a specific gravity of 1026 to 1033, a small trace of albumin, numerous hyaline and occasional granular casts, and 2 to 5 red blood-corpuscles per high-power field. White count 12,400; hemoglobin 80 per cent.; differential count normal. Wassermann reaction negative.

The electrocardiogram showed a rate of 120, with frequent ventricular premature beats, at times bigeminal, also probably intraventricular block.

In spite of rest in bed and digitalis the patient grew steadily worse and died seven days after admission.

Several interns saw the case, and each one made a diagnosis of rheumatic heart disease with mitral stenosis and aortic regurgitation and adherent pericardium. The case was seen by two consultants. One opinion was: "Acute endocarditis in an old rheumatic heart, with mitral stenosis, aortic regurgitation, adherent pericardium, and congestive failure. Arrhythmia due to frequent ventricular premature beats, at times bigeminal. Very big heart." The other consultant said: "Chronic infection of mitral and aortic valves, with extensive cardiac hypertrophy. A Broadbent well marked, and I believe adhesive pericarditis may be a factor in the production of the very extensive cardiac enlargement."

*Autopsy:* The heart was the chief interest in this case. Its weight was 905 grams, greatly enlarged. Right ventricular wall 4 mm. thick; left ventricular wall 13 mm. thick. Left ventricle showed marked dilatation; right ventricle moderate dilatation. Mitral valve circumference 12 cm. The mitral curtain showed a slight amount of thickening along the free margin and in two or three places there were minute fibrous tags. Otherwise the mitral valve was negative. \*

The aortic valve circumference was 10 cm. The free margins of the aortic cusps showed small crescentic fibrous plaques. The surfaces of these were a little irregular and the free margins showed minute, firm, grayish granules. Otherwise this valve was completely negative.

There was a mural thrombus of the right ventricle. Chronic adhesive pericarditis was present.

Other findings of interest were small infarcts in the lower lobes of both lungs; congenital absence of the left kidney with hypertrophy of the right; and embolic thrombosis of small branches of the pulmonary artery.

Microscopic examination of the myocardium showed little or no degeneration. The thrombus from the right ventricle showed some organization.

*Discussion:* This case is a striking illustration of the difficulty involved in making an accurate diagnosis of heart disease in the presence of marked cardiac hypertrophy. History and physical findings both favored the diagnosis of valvular damage which was not confirmed at autopsy. The chronic adhesive pericarditis explains the cardiac hypertrophy. The mitral diastolic murmur in this case is probably to be explained by the marked dilatation of the left ventricular cavity. It is likely that a normal mitral valve plus a much dilated left ventricle acts in the production of a mitral diastolic murmur in the same way that a stenosed mitral valve acts with a left ventricular cavity of normal size. It is possible that this theory of relative stenosis is the true explanation, as has been suggested already, for the Austin Flint murmur of the "functional mitral stenosis" of marked aortic regurgitation, instead of the pressure on the anterior cusp of the mitral valve by the regurgitant stream of blood re-entering the left ventricle from the aorta. It would be of interest to determine if the Austin Flint murmur is present only in those aortic regurgitant hearts with dilated left ventricles, since not infrequently the Austin Flint murmur is absent even with pronounced aortic regurgitation. In the present case under discussion the murmur should not probably be considered an Austin Flint murmur, since the aortic regurgitation was slight, and since the aortic valve was essentially normal at postmortem examination. The further question comes up as to the cause of the apparent aortic regurgitation in this case. It may be one of the rather rare functional aortic regurgitant cases.

One other feature here should not pass unnoticed. What would have been the course of events had the tonsils been removed with the first attack of rheumatic fever at ten years of age? Certainly subsequent attacks of tonsillitis would have been avoided, and these were many. Possibly some or all of the five subsequent attacks of rheumatic fever would have been avoided. It is quite probable that the early removal of the tonsils would have favorably influenced the prognosis by years.

**Case II.** *Cardiac Hypertrophy and Dilatation. Cause Unknown, Possibly Syphilitic. Mitral Valve Normal.*—This case illustrates very forcibly the same points as the preceding case.

J. F. A white man of forty-eight years entered the hospital September 25, 1922 for weakness and dyspnea with a provisional diagnosis of "cardiac mitral stenosis (?), also central nervous system lues (?)."

*Present illness:* The patient complained of dyspnea and weakness for a week before entrance. Palpitation on exertion and moderate edema of the feet both came on at this time. No symptoms whatever before.

*Past history:* No scarlet fever, tonsillitis, rheumatic fever, or chorea. Gonorrhea twenty-five years ago with "rheumatism" following it, which kept him in bed for one and a half years. He denied syphilis by name and symptom. His memory had been failing for several years and there was an indefinite history of fainting attacks years ago. Two years before entrance the patient was diagnosed "iritis" at the Massachusetts Eye and Ear Infirmary and was sent over to the Out-patient Department of the Massachusetts General Hospital for study and treatment. The possibility of a specific iritis was considered, but there were three negative Wassermann reactions and no improvement resulted from treatment. The blood-pressure at this time was 120 mm. of mercury systolic and 60 mm. diastolic. A chronic prostatitis was found. There is little else of importance in the past history.

*Physical examination:* "A well-developed and nourished man with marked cyanosis of the skin and mucous membranes." The left pupil was larger than the right and did not react to light or distance. There was an opacity of the left lens. Radials were thickened. Palpation of the abdomen was unsatisfactory. Knee-jerks exaggerated, right greater than left.

Heart: "Markedly enlarged. Apex impulse in the fifth interspace 13 cm. to the left. Substernal dulness 7 cm. Blowing systolic and low rumbling diastolic murmurs localized at the apex. A diastolic whiff follows second sound at third left interspace. Pulmonic second sound accentuated."

The pulse was 90 to 100. The temperature was 100° to 100.5° F. The blood-pressure was 130 systolic and 60 diastolic.

The urine showed a specific gravity of 1028, a small trace of albumin, and 20 to 30 pus-cells per high-power field. The white count was 18,400, red count, 5,300,000, polynuclear leukocytes rather high—85 per cent. The blood Wassermann reaction was negative. Lumbar puncture showed a clear fluid at rather high pressure, cells none, alcohol ring test positive, ammonium sulphate test negative, total protein 37 (normal), spinal fluid Wassermann reaction negative, gold sol. curve 0000000000.

On the second day after admission the patient suddenly became unconscious and very cyanotic, dying in a few minutes.

The intern's diagnosis, evidently based largely on the heart murmurs present, was: "Question of central nervous system syphilis. Aortic regurgitation and mitral stenosis. Acute myocardial failure."

The case was also seen by a consultant, who made the following note: "Heart large, with poor quality of sounds and gallop rhythm. Aortic sounds very faint; short early diastolic murmur at the aortic area. Diastolic rumble at apex. Why? Not typically mitral stenosis, though some sort of rheumatism occurred years ago. Undoubtedly lues is a factor, aortitis, perhaps mediastinitis, or aneurysm."

*Autopsy:* Heart. The organ weighed 550 grams. Right ventricular wall 4 mm. in thickness. Left ventricular wall 12 mm.

The left ventricle showed considerable dilatation. The circumference of the mitral valve was 11 cm., that of the aortic,  $7\frac{1}{2}$  cm. All valves were completely negative. The pericardium was negative. The aorta showed a slight amount of fibrous sclerosis, but no report of any dilatation was made. No evidence of lues. The left coronary artery was pipe-stem in character and practically occluded at points.

Some general chronic passive congestion was present. There was slight bilateral hydrothorax (300 c.c.) and slight ascites. The brain and spinal cord were not examined.

Microscopic examination of the myocardium and kidneys was negative.

**Discussion:** Another case is presented in which a functional mitral diastolic murmur in an enlarged heart led to an incorrect diagnosis of valvular heart disease.

In this case a satisfactory explanation of the cardiac hypertrophy is difficult. Lues may have been the cause in spite of the negative findings. An essential hypertension may have been present earlier in life leading to cardiac hypertrophy. Occasionally a large heart comes to postmortem examination with no satisfactory explanation. It is interesting to note the definite partial occlusion of the left coronary artery without a history of heart pain. This occlusion cannot explain the cardiac hypertrophy.

**Case III. Cardiac Hypertrophy and Dilatation. Cause Unknown, Possibly Rheumatic. Mitral Valve Normal.**—A short statement of this case is given to illustrate further deceptive apical murmurs in large hearts, and to show it is unwise to make a diagnosis of mitral stenosis without the pathognomonic diastolic murmur.

H. K., a white man of forty-two years entered the hospital March 27, 1921, complaining of shortness of breath of two months' duration and of sharp attacks of precordial pain. He had had several attacks of rheumatic fever in childhood and also attacks at nineteen and thirty-one years of age. The patient ran a temperature from  $99^{\circ}$  to  $101^{\circ}$  F. and a pulse of 100 to 110. His blood-pressure was 100 mm. mercury systolic and 70 mm.

diastolic, 105 and 80, and 110 and 80 on three different occasions while on the ward at the Massachusetts General Hospital. His electrocardiogram was normal except for small ventricular complexes in all leads and a diphasic T wave in Lead II. He gradually grew weaker and more dyspneic, and finally died on the eighteenth day after entrance.

The chief feature on physical examination was a marked increase in the transverse diameter of the heart. Two consultants saw the case and the sounds are best described by them. One made the following note: "Rheumatic heart disease, chronic and acute, with mitral stenosis. At present recurrent rheumatic carditis in progress. Protodiastolic gallop rhythm. In the presence of the weak heart action there is no mitral diastolic present today. Mitral facies and prominence of left auricle by percussion."

The following is another note by the same consultant eleven days later: "Heart rate continues rapid and regular. Apex impulse in axilla; auscultation here shows a gallop rhythm, with probable diastolic rumble. Still believe mitral stenosis present."

A second consultant wrote: "Present feature is a wide cardiac dulness with weak heart sounds. Am more inclined to a rheumatic etiology than a degenerative one based on arterial impairment. Possibly under digitalis and rest more evidence of mitral disease will appear."

*Autopsy:* The heart weighed 703 grams, greatly enlarged. Cavities all showed marked dilatation.

Mitral valve circumference 15 cm. Without lesions. Aortic valve at cusps 8 cm. In the regions of their conjoined margins they presented a short, rounded ridge of fibrous thickening. There were only two large cusps; otherwise negative. There were mural thrombi in the right auricle and left ventricle. Pericardium negative.

Other findings of interest were small infarcts in the lungs; an infarct in the left kidney; right hydrothorax, slight ascites, and chronic passive congestion.

Microscopic examination of the myocardium showed fibrous myocarditis.

Discussion: A case with cardiac hypertrophy and a questionable diastolic rumble at the apex on auscultation, without deformity of valves on subsequent postmortem examination. In the absence of the pathognomonic middiastolic rumble of mitral stenosis it is unwise to make that diagnosis.

Here again the cause of the cardiac hypertrophy is obscure. With normal kidneys (with the exception of a small infarct) and with such a low blood-pressure a hypertensive etiology seems unlikely. The definite history of several attacks of rheumatic fever certainly make rheumatic myocarditis a possibility, although it is improbable that it is the sole etiologic agent of cardiac hypertrophy.

**2. Diastolic Murmurs Almost Certainly Present, but Overlooked, with Definite Mitral Stenosis at Autopsy.**—Sometimes the diastolic murmur of mitral stenosis is not heard by some observers when it is present. Cabot<sup>9</sup> has noted that out of 130 cases, in which the lesion was found at autopsy at the Massachusetts General Hospital for the two decades following October, 1895, only 73, or 56 per cent., were recognized during life. In recent years, however, there has been apparently a marked improvement in the diagnosis of mitral stenosis in this hospital. From January 1, 1917 to January 1, 1923 out of 774 autopsies there were 23 instances of definite stenosis of the diseased mitral valve, with a valvular circumference of  $7\frac{1}{2}$  cm. or less. Of these, 19, or 82 per cent., were diagnosed correctly antemortem. A mitral valve circumference of  $7\frac{1}{2}$  cm. may fairly be considered the borderline between the slighter degrees of mitral stenosis, largely of academic interest, and those of clinical importance. If every case of organic mitral involvement is called mitral stenosis, many will be missed in clinical diagnosis, which might be labeled "very slight stenosis" at autopsy.\*

\* It may be that occasionally valve vegetations, which do not actually produce mitral stenosis, may cause a diastolic murmur.

It is also noted that the number of special workers around the hospital is increasing and that not infrequently many doctors examine one case. In addition, if a heart condition is suspected, some one especially interested in cardiac problems sees the patient as a rule. These factors have tended to diminish the chances for error in diagnosis. However, the failures to diagnose mitral stenosis during life are still sufficiently frequent in this hospital and elsewhere to make a discussion of this condition worth while.

It is of great interest to note that as early as 1828 to 1835 Charles J. B. Williams<sup>16</sup> of London described fairly well the mitral diastolic murmur, at the same time correcting Laennec's idea of the diastolic filling of the ventricles. He wrote as follows: Obstructive disease of the mitral valve "may cause a murmur with the diastole of the ventricle, and, therefore, at the time of the second sound; for although the ventricle in itself produces no sound, yet, when the orifice, by which it becomes re-filled is contracted, the current being partially resisted in passing through, may become sonorous. This will, therefore, leave the result much as Laennec represented it, inasmuch as there is a current from the auricles to the ventricles during the diastole of the latter, although this current is not produced as he supposed, by the contraction of the auricles. But the results of my late experiments must modify the statements of both M. Laennec and Dr. Hope in this respect, that the contraction of the mitral orifice with its impeded current and attendant murmur, will not necessarily supplant the second sound, inasmuch as this sound is seated in the semilunar valves, the action of which may still be perfect."

Gairdner<sup>10</sup> in 1861 explained more fully the diagnostic significance of the diastolic murmur of mitral obstruction. He described accurately with diagrams the position of this murmur in late diastole running up to the first sound, and its significance. In the sixty-two years that have elapsed since this time many have contributed to our knowledge of mitral stenosis. Chief among these are Graham Steell and Sir James Mackenzie.

There are several features of interest in a discussion of the

auscultatory findings in mitral stenosis. It is the experience of this clinic<sup>11</sup> that mitral valve damage is proved only by a diastolic murmur at the apex, which begins a brief interval after the second heart sound, in the absence of an early diastolic murmur heard along the left sternal border, and in the absence of marked dilatation of the left ventricle. There may or may not be a presystolic crescendo murmur at the end of it and a diastolic thrill may or may not be present. Both of these last-named findings occur only with well-marked stenosis. This characteristic murmur occurs after the usual time of the third sound and is low pitched and rumbling. It is best heard at or just inside the maximal apex impulse. It cannot be emphasized too strongly that the examination be made with the patient in the recumbent position and by the bell stethoscope. Especially in children failure to do this may mean failure in the diagnosis of early mitral stenosis. In any doubtful case the patient should be examined recumbent after exercise.

Other auscultatory signs that may be present are marked accentuation of the second sound at the second left interspace ( $P_2 ++$ ), a sharp first sound at the apex relatively frequently, sometimes a reduplication of the first sound, and a prominence of the third heart sound. This last should always inspire a search for a middiastolic murmur following the third sound. A pronounced presystolic murmur alone without the middiastolic murmur has been a rare finding in this clinic.<sup>11</sup> The presystolic accentuation of the diastolic murmur of mitral stenosis disappears in auricular fibrillation, leaving only the middiastolic murmur. Hence it is wiser to rely on the earlier diastolic murmur rather than on the presystolic in the diagnosis of mitral stenosis. Sewall<sup>12</sup> sounded a note of warning against the presystolic murmur as an absolute diagnostic sign in mitral stenosis when he concluded that the structurally normal heart may produce a sound similar to the presystolic murmur heard in certain stages of mitral stenosis.

A case is reviewed here in which the diastolic murmur of mitral stenosis was missed by some examiners.

**Case IV.** *Cardiac Hypertrophy and Dilatation. Rheumatic Heart Disease. Mitral Stenosis.*—J. M. A white man forty-four years of age first entered the Out-patient Department of the Massachusetts General Hospital in June, 1912, complaining of dyspnea and cough on slight exertion.

The patient had definite rheumatic fever at the age of fourteen and again at forty-two. He also had scarlet fever in childhood. For years he had had a "winter bronchitis," but the additional symptoms of dyspnea for some weeks before entry brought him to the Out-patient Department in June, 1912. When he was examined at this time his heart showed enlargement, irregularity, and a "mitral regurgitant murmur." A diagnosis of mitral regurgitation and myocarditis was made.

The patient was not seen again until May, 1914. At this time he showed a marked increase in dyspnea and there was also edema of the feet. He was referred from the Out-patient Department into the hospital wards for study and treatment. It there developed that one year before entrance an attack of dyspnea, cough, and palpitation of ten days' duration had occurred. Again, two and a half months before entrance to the wards, he had had a similar attack, this time with blood-spitting and edema of the feet. A recurrence of the dyspnea and edema of the feet was the cause of his admission to the hospital wards May 14, 1914. Examination of the heart while in the hospital showed an enlarged heart, "a blowing systolic murmur at the apex transmitted to the left axilla, and a faint diastolic murmur along the left sternal border." There was no record made of any diastolic murmur at the apex. The pulmonic second sound was accentuated. Moderate congestive failure was present. A diagnosis was made of "chronic endocarditis of the mitral valve and emphysema." The patient was discharged May 27, 1914.

The patient improved rapidly under digitalis. He was next seen in the summer of 1914, when a polygraphic tracing showed auricular fibrillation. He was not seen again until February, 1915. At this time in the Male Medical Out-patient Department of the Massachusetts General Hospital a low rumbling mid-

diastolic murmur at the apex was heard for the first time, and a diagnosis of mitral stenosis and auricular fibrillation made. Electrocardiogram confirmed the irregular rhythm.

Not until January, 1917 did serious congestive failure again occur, and then the patient was again sent into the hospital wards for treatment. This time both the irregularity and a low pitched diastolic murmur at the apex were noted, and a diagnosis was made of "mitral stenosis, decompensated, and auricular fibrillation." The patient was again discharged to the Out-patient Department and for a short while did moderately well. Gradually the short episodes of slight congestive failure became more and more frequent, and finally he was again referred to the hospital wards on January 12, 1920 with ascites, edema of the feet, and moderate left hydrothorax.

Examination by the intern in charge now showed an enlarged heart, absolute irregularity with an apex rate of 70, a soft systolic murmur at the apex, and an accentuated pulmonic second sound. There is no record of any diastolic murmur at this examination. This intern made a diagnosis of generalized arteriosclerosis, cardiac hypertrophy, and decompensation. He failed to make any mention of valvular disease. A second intern saw the case frequently and made several notes, but also failed to discover a valvular lesion. On February 11, 1920 the ward consultant examined the patient and made the following diagnosis: "Chronic valvular heart disease, mitral stenosis, auricular fibrillation, myocardial insufficiency, and arteriosclerosis."

The patient was well digitalized; various diuretics were tried; thoracentesis was done. All of these failed to relieve, and the patient took a progressive course downward and died February 15, 1920 after five weeks in the hospital.

*Autopsy:* The heart weighed 660 grams. Right ventricular wall 7 mm. thick; left ventricular wall relatively thin—8 mm. Left ventricle considerably dilated; left auricle showed marked dilatation. The right ventricle and right auricle showed marked dilatation. Adherent thrombotic mass in the left auricle. The mitral valve presented a crescentic orifice about  $1\frac{1}{2}$  cm. long

(marked stenosis). The valve showed great fibrocalcareous deformity, with shortening and thickening of the chordæ tendineæ, and great decrease of the orifice. It was somewhat "fish-mouthed" in appearance. The other valves were essentially negative except for a slight chronic endocarditis of the aortic valve.

Other findings of interest were chronic passive congestion, hydropericardium (200 c.c.), hydrothorax (1000 c.c. in each pleural cavity), ascites, and small infarcts in both lungs.

**Discussion:** The point of interest in this case is the failure of several different examiners to hear or at least to interpret properly the characteristic low-pitched diastolic apical rumble of well-marked mitral stenosis. The presence of auricular fibrillation, of course, prevented the accentuation of the presystolic part of the murmur at a moderately slow heart rate. Anyone hesitating to make a diagnosis of mitral stenosis except in the presence of a presystolic murmur would, of course, miss the mitral stenosis here, and yet without regard to rhythm this old rule is still largely followed by the medical profession. As a matter of fact, whatever the rhythm may be, the earlier phase of the diastolic rumble is more essential for diagnosis than its later or presystolic phase so often absent even with normal rhythm.

#### B. CERTAIN SYSTOLIC MURMURS AT THE BASE OF THE HEART

**1. Systolic Murmurs Leading to a Diagnosis of Aortic Stenosis Not Confirmed at Autopsy.**—Cabot says: "During life the diagnosis of aortic stenosis is frequently made, but often on insufficient evidence—*i. e.*, upon the evidence of a systolic murmur heard with maximum intensity in the second right intercostal space and transmitted into the vessels of the neck."<sup>18</sup> This observation is based on a review of 3000 clinical and autopsy records of the Massachusetts General Hospital from October 19, 1895 to February 12, 1912. In 1307 cases, however, which came to postmortem examination at the same hospital in ten years from January 1, 1913 to January 1, 1923 there was no case diagnosed aortic stenosis clinically which failed to show this

lesion at necropsy. Apparently as we have become more zealous in diagnosing mitral stenosis we have, on the other hand, become more wary in the diagnosis of aortic stenosis. The presence of a palpable thrill at the base of the heart, a small plateau pulse, and the absence or diminution of the aortic second sound, in addition to a rough systolic murmur over the aortic area, have probably been demanded for the diagnosis of aortic stenosis in a given case. A diagnosis depending on a basal systolic murmur alone, however loud it may be, is always unreliable.

Up to the present time many writers have considered roughening of the aortic valve or intima of the aortic arch as the cause of a systolic murmur heard over the aortic area. Reid<sup>14</sup> has recently reviewed 80 autopsies from the medical services of the Boston City Hospital, and in 18 of these cases ". . . the aortic (valve) was disclosed to be definitely roughened from various sclerotic changes, in most of which calcification was present, and yet no systolic murmur at the base was recorded." Measurements comparing the aortic valve circumference and the circumference of the first portion of the aorta should be made in cases with and without systolic murmurs over the aortic area. It seems reasonable that such measurements would show a relative narrowing of the aortic circumference compared to a dilated aorta beyond. This might well explain most of the aortic systolic murmurs formerly ascribed to arteriosclerotic valve roughening. From the literature and from his own experimental work Reid concludes: "Roughness of the inner surface of a vessel appears not to be a cause of a murmur, or if this be not literally true, then a murmur due to roughness of the vessel wall is very slight and in no sense comparable to those produced when a *veine fluide* or culdesac against the stream are present."

**2. Systolic Murmurs Along with Other Findings Leading to a Diagnosis Other Than Aortic Stenosis with Aortic Stenosis at Autopsy.**—Taking the converse of the above, we find that in spite of an increasing wariness the diagnosis of aortic stenosis

is made correctly in a good percentage of cases coming to necropsy. In the 1307 autopsies in the ten years from January 1, 1913 to January 1, 1923 at the Massachusetts General Hospital there were 19 cases with definite organic disease of the aortic valve and a valvular circumference of 6 cm. or less. These were considered to have aortic stenosis at autopsy. Of these 19 cases, 10 were correctly diagnosed clinically. Of the 9 cases that were missed clinically, 3 had aortic orifices with a circumference of  $5\frac{1}{2}$  to 6 cm., which is apparently the borderline of stenosis clinically demonstrable in the adult heart; one of these three and three others were very ill when examined, and showed weak, generally rapid heart action. In 3 cases only may the errors be considered as inexcusable. One of these 3 cases is given here, in which an attempt was made to explain the systolic murmur heard over the aortic area by "valve roughening."

**Case V. Cardiac Hypertrophy and Dilatation. Cause Probably Rheumatic. Aortic Stenosis.**—M. T. (E. M. 208,607). A white housewife of fifty-five years entered the Massachusetts General Hospital May 25, 1916 for dyspnea and edema of the feet.

**Present illness:** Eighteen months ago the patient had an attack characterized by orthopnea and edema, beginning in the ankles and soon occurring over the entire body. She sat in a chair for eleven months. There was occasional precordial distress. A local doctor put "tubes into her legs," with considerable relief of the edema. After these eleven months she went to the Peter Bent Brigham Hospital for eight weeks, where she was further relieved.

Three months ago, following an acute respiratory infection, the previous symptoms returned, and she has been in bed with some orthopnea and edema ever since.

**Past history:** The patient had pneumonia three years before entrance, and measles and diphtheria during childhood. No history of rheumatic fever or chorea. No tonsillitis except one attack, with peritonsillar abscess, seven years before entrance. For months she had had frequent urination during the

day and about every two hours at night. Otherwise there was nothing striking in the past history.

The family and marital history are of some interest. Her father and one brother died with "Bright's disease." Her mother and one son died with "diabetes." The patient's first husband died with "cardiac disease."

*Physical examination:* "The patient is an exceedingly obese woman (weight, 296 pounds), making examination difficult. Some cyanosis present; moderate orthopnea."

Heart: "Apex impulse not seen or felt, but the heart is apparently considerably enlarged to the left by percussion. The sounds are regular, distant, slow, and of good quality. There are no thrills and no murmurs. The pulse is of fair volume and tension. The brachial arteries are not tortuous."

No râles were made out in the lungs and the liver edge was not felt. There was considerable edema of the shins. Otherwise the physical examination was not remarkable.

The pulse varied from 80 to 100. The temperature was normal. The blood-pressure was 152 mm. mercury systolic and 115 mm. diastolic.

The urine showed specific gravity of 1010 to 1020, a very slight trace of albumin on two out of four examinations, 5 and 8 grams of glucose in two respective twenty-four-hour specimens. The white blood-count was normal, hemoglobin 75 per cent. The Wassermann reaction was negative. A renal functional test (phenolsulphonephthalein) was 25 per cent. in two hours and ten minutes.

The electrocardiographic findings were: An occasional ventricular premature beat, heart rate 90, left axis deviation, an inverted T wave in Lead II, and a question of intraventricular block.

Digitalis (powdered leaf), gr. iss t.i.d., was begun in the hospital on March 28th. On March 27th a systolic murmur was noted over the aortic area, but no further note was made about it. The patient seemed to be doing fairly well until March 29th, when with some slight exertion in bed she became quite cyanotic and died in a few seconds.

The following clinical diagnosis was made: "Chronic myocarditis, with cardiac failure, aortic roughening, arteriosclerosis, chronic interstitial nephritis, glycosuria, and obesity.

*Autopsy* (No. 3610): Heart. This organ weighed 872 grams. There was marked hypertrophy and dilatation of the left ventricle. The mitral valve was normal. The aortic valve was represented by a triangular slit which just admitted the closed blades of an enterotome. The aortic cusps showed marked fibrous and fibrocalcareous degeneration, with fusion and great deformity of the cusps. Coronary arteries free and capacious.

Other findings of interest were slight arteriosclerosis, chronic passive congestion, moderate bilateral hydrothorax, arteriosclerotic and acute degeneration of the kidneys, hemorrhage and necrosis of the pancreas, and chronic interstitial hepatitis.

*Discussion:* A case of marked aortic stenosis not recognized during life is presented. It is true that the patient was quite obese, thereby making examination of the heart inaccurate and difficult. However, there was a systolic murmur at the aortic area which apparently led to a diagnosis of aortic valve roughening. It has already been said above that roughening alone of the aortic valve is probably not a cause of a loud systolic murmur at the second right intercostal space. The low pulse-pressure is noteworthy in this case, and should, together with the character of the pulse, have suggested the correct diagnosis. No record was made of the character of the aortic second sound, which was probably diminished or absent. The marked cardiac enlargement may have been due in part to a long-standing hypertension.

#### SUMMARY

1. Diastolic murmurs may occur in certain large hearts with normal valves and lead to a false diagnosis of mitral stenosis. Left ventricular dilatation of high degree seems to be the main factor in such cases, and may perhaps also explain the Austin Flint murmur which is heard only in certain cases of aortic regurgitation.

2. Failure to diagnose mitral stenosis in most instances is

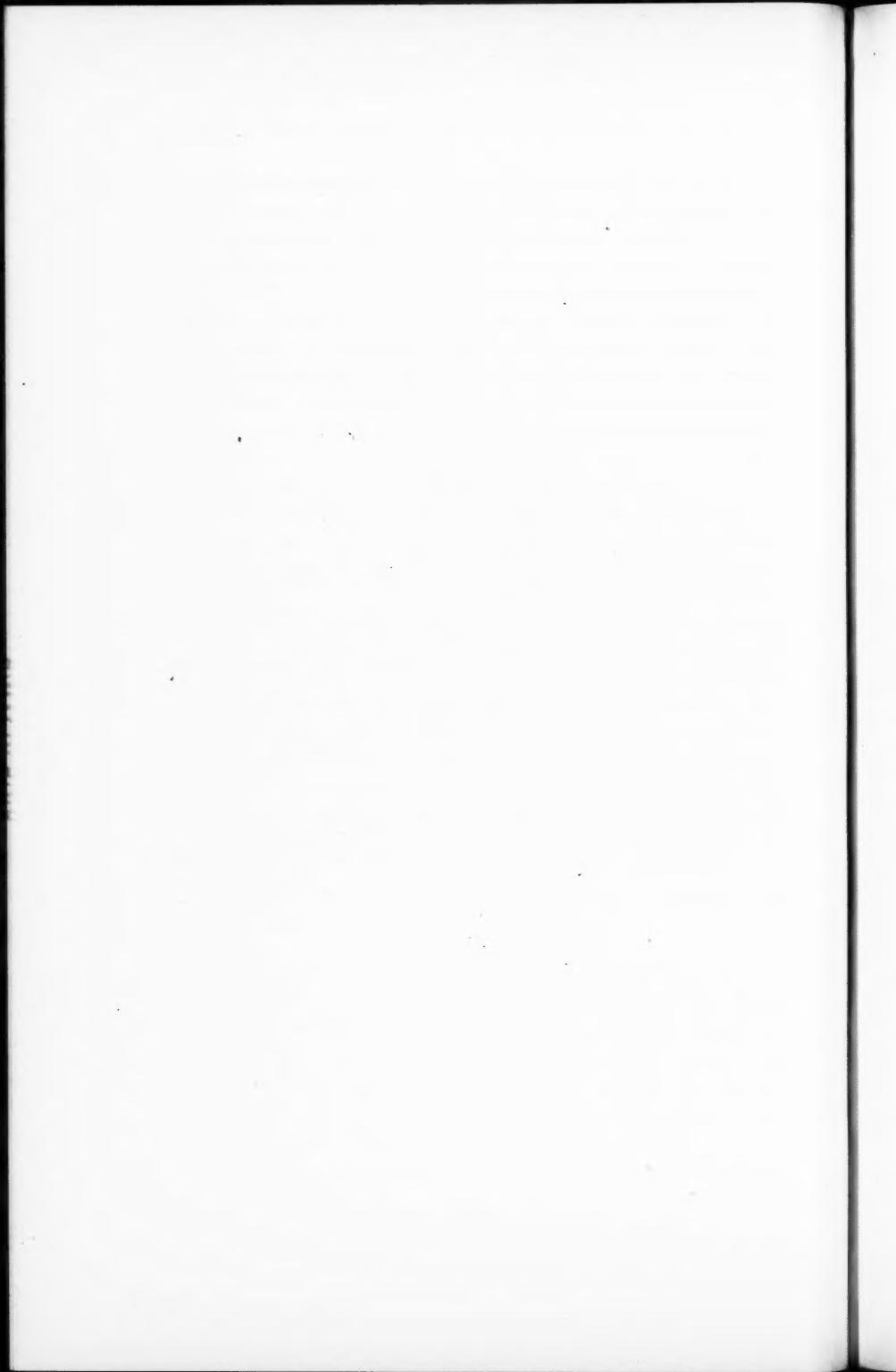
probably due to failure to hear or to interpret correctly the pathognomonic apical middiastolic rumble of that lesion.

3. A clinical diagnosis of aortic stenosis, when not present postmortem, has not occurred at the Massachusetts General Hospital in the past ten years.

4. Failure to diagnose aortic stenosis when present may be due in part to a lack of careful observations of the classical signs, and in part to an attempt to explain some loud systolic murmurs over the aortic area as valve roughening, even though thrill and pulse change be present.

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## CLINIC OF DR. FRITZ B. TALBOT

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### CYCLIC VOMITING

In this clinic I am going to discuss one of a series of characteristic cases of cyclic vomiting.

This patient, a girl of seven years, was first seen at the age of three and a half years. She had been perfectly well up to the age of three years except for constipation and, at times, gray colored stools. She then became irritable, cried out in her sleep at night, and was difficult to manage.

The physical examination at this time was negative. It was found that the stools contained an excess of fat. Considerable improvement was noted after reducing the fat in the food.

She was seen again two years later at the age of five and a half years with a history of repeated attacks of nausea and vomiting associated with fever. The constipation still persisted, and when she had a movement it was very large. At times there were two movements a day.

The attacks of nausea and vomiting came on about once a month and lasted from two to four days. Preceding an attack she looked tired and fagged out.

She had considerable nervous energy and wanted to be on the "go" all the time, despite the fact that she became easily tired.

The physical examination at this time showed a well-developed and fairly nourished child. Her color was fair, but she looked fatigued. Her mouth and throat were normal; the tonsils were not enlarged. The heart, lungs, and abdomen were normal except that the abdomen was protuberant and pendulous, and the musculature of the abdominal wall was very weak, especially

in the lower part. The back was fairly straight. The liver and spleen were not palpable.

The urine was of normal color, clear, and the specific gravity was 1022. It was very acid, but contained no albumin, sugar, or acetone. The sediment was negative.

The stool was brown, semiformed, slimy, fairly well digested. There was no meat or starch, but still an excess of fat.

A diagnosis of cyclic or recurrent vomiting and improper posture was made.

An anteroposterior pad and support for the lower abdomen<sup>1</sup> was fitted by an orthopedist. Instructions were given the parents for rest and exercises to correct the enteroptosis, and a further reduction was made of the fat in the diet.

Three months later she reported, and in the interim had only had one attack of vomiting. There was a marked improvement in her appearance; the fatigued expression had gone. The eyes were brighter and more alert and the lines had disappeared from under them. Her color was very much better, and the musculature, instead of being flabby, was moderately firm. On the whole, she looked like a different child, and in general health had not been so well since two years of age. She now reports, after a lapse of three years, and has had no recurrence of symptoms.

On leaving off the support, however, she becomes tired and fretful and there is a slump in the posture.

This case is an example of the therapeutic effect of an abdominal support in a case of constipation with bad posture and recurrent or cyclic vomiting.

Cyclic vomiting is a relatively frequent condition in childhood. It is characterized by periodic attacks of vomiting recurring at fairly regular intervals. The attacks are usually of two or three days' duration, although at times the vomiting may persist for six or seven days. Attempts to control the vomiting are frequently without avail, the attack usually stopping of its own accord.

<sup>1</sup> Talbot and Brown: Amer. Jour. Dis. Child., 1920, 20, 168.

The onset of attacks is usually between the ages of two and four years. This is of especial interest if the disease is to be considered as secondary to poor body mechanics, that is to say, poor posture. Up to the second year of life a child spends the greater part of the twenty-four-hour day lying prone, and it is not until after this time that defects in posture have an opportunity to manifest themselves.

These attacks generally come out of a clear sky, in the midst of apparent health. As a general rule in all these cases there is a history of constipation. There is a heavily coated tongue and sometimes fever with the vomiting. Everything taken by mouth, even water, is rejected, and in a short time, unless measures are taken to counteract this, the body becomes dried out. In some cases the desiccation becomes so great that symptoms of an acidosis, such as cherry red lips and air hunger, appear. As the body becomes dried out the urine becomes concentrated and may contain small traces of albumin and hyaline casts. It nearly always contains the ketone bodies, acetone, and diacetic acid. These may sometimes appear before the vomiting commences. The odor of acetone may also be detected on the breath.

The attacks are not, as a rule, connected with errors of diet. They are, however, frequently precipitated by unusual excitement, such as a children's party. Careful observation may show that a diminution in the elimination of fecal material occurs a day or so preceding the attack. Occasionally an attack ends with a very large bowel movement in which a large mass of fecal material is discharged.

One case of cyclic vomiting stands out very prominently, in which the child vomited for five days steadily, and on the sixth day, after a very large bowel movement, sat up and said, "I am well, I want something to eat." She then ate a heavy dinner without any harmful effects.

Many explanations have been given of the cause of cyclic vomiting. In some instances the attacks of vomiting have been thought to have been brought on by colds or infections of the nasopharynx, and certain cases have been reported to have

been cured by a removal of the tonsils, while in others this procedure has had no effect at all. In cases where tonsillectomy has been followed by cessation of attacks it has probably been due to the beneficial effect of removal of the tonsils in preventing infection.

Occasionally symptoms of cyclic vomiting simulate those of tabes mesentericus, but in the latter there is more frequently pain and other evidence pointing toward a tuberculous infection.

In all cases of recurrent vomiting it is necessary to rule out the question of a chronic appendix. Recurrent attacks of chronic appendicitis are often confused with cyclic vomiting, and if overlooked may terminate fatally.

The presence of the acetone test in the urine and the smell of acetone on the breath during nearly all attacks of cyclic vomiting has led many writers, especially the French, to associate acetonemia and the vomiting. Marfan, the principal French writer on this subject, admits, however, that there is no evidence that the ketone bodies produce an attack, since they are found in many other affections. The evidence is more in favor of the fact that these bodies are either due to the fasting or to some abnormality in the fat metabolism. The presence of fat in the stools and the frequency of enlargement of the liver in these cases points toward the latter as the more plausible explanation.

It is still a great question whether the acidosis appears early in these cases. It is probable that the diminution in the alkali reserve of the body does not take place except in prolonged attacks. If enough liquid is gotten into the body, and there is no desiccation, the ketone bodies do not accumulate in large enough amount to diminish any of the alkali reserve. It is not necessary here to go into a discussion of the treatment of true acidosis as long as the kidneys are working and the ketone bodies are being excreted and are not accumulated in the body, there is little or no danger of acidosis. If, on the other hand, they are not washed out or excreted they accumulate in sufficient concentration to result in an acidosis requiring treatment.

The most satisfactory treatment is to treat the cause of the

acidosis. It is customary in some places to give large amounts of bicarbonate of soda. This may be indicated when the alkali reserve of the blood is diminished, but it does not reach the cause of the diminution; the cause being an excessive amount of ketone bodies circulating in the blood. As in diabetes, the administration of glucose intracutaneously or intravenously will prevent the formation of ketone bodies.

There is also a lack of assimilation of fat associated with cases of cyclic vomiting. More than a normal amount of fat is generally found in the stools of children with pronounced ptosis. With the correction of the poor posture the fat usually disappears from the stools, so that one is forced to assume that the presence or absence of ptosis has something to do with the assimilation of fat in these cases. As a rule after the posture has been corrected these children are able to take two to three times as much fat as formerly.

Fatigue always plays a very important part in these cases and goes hand in hand with improper body mechanics, making a vicious circle. Both these conditions must be corrected before satisfactory results are obtained.

In 1920<sup>1</sup> Brown and I reported a series of cases of cyclic vomiting, and since this time have studied many additional cases. The one physical finding common to all these cases is bad posture. Persistent efforts to correct the poor body mechanics have resulted in a lessening and eventually a cessation of the attacks.

As I have already stated, a history of severe constipation and poor posture is common in nearly all cases of cyclic vomiting. Even though the bowels move daily, it does not necessarily mean that there is a complete evacuation of the fecal material. It seems probable that in these cases there is what might be termed "fractional constipation," that is, incomplete evacuation which allows an accumulation of fecal remains sufficient to cause an attack of vomiting. The fact that large amounts of fecal material are often evacuated at the end of an attack of cyclic vomiting which has lasted several days is taken as evidence of this point of view.

Treatment in cases of cyclic vomiting should be based upon prevention of fatigue and correction of the body mechanics. Fatigue should be avoided by carefully regulating the habits, by suitable rest periods, and by getting the required amount of sleep. In the beginning in these cases it is often necessary to prescribe two one-hour rest periods during the day. Modifications of this régime are, of course, necessary in the case of school children. After a sufficient length of time of this routine they are able to carry on their ordinary duties with one hour's rest during the day.

It is also necessary in these cases to avoid fatigue of the digestive organs. This may be done by giving only the most digestible types of food and the digestion controlled by examination of stools. Ordinarily these cases do better on a low fat diet until such time as the ptosis has been corrected. It is a curious fact that fat in the form of butter is less harmful than fat in the form of cream. It is often possible to take two to three butter balls a day without causing symptoms.

Because of the peculiar tendencies of acetonuria and the symptoms that come with it, it is important that the diet should contain a sufficient amount of carbohydrate to supply enough antiketogenic factors to prevent the appearance of acetone. It is very important that all the starches should be thoroughly cooked, as uncooked starches are not easily absorbed.

Correction of body mechanics: The body mechanics if left untreated tend to adjust themselves when the child reaches the age of ten or eleven years, at which time growth changes preceding puberty set in. Some time during this period the normal natural exercises develop the musculature even in weak places, the body commences to assume the adult shape, and there is a natural tendency for the sagging abdomen to right itself by the normal growth and exercise of the unhampered child. This I have taken to be consistent with the mechanical explanation of cyclic vomiting.

Improper body mechanics adds to the muscular strain on certain parts of the body and results in fatigue. Fatigued muscles, on the other hand, are conducive to bad body mechanics.

If a child is tired and fatigued, the muscles become tired and do not work properly.

In cases of cyclic vomiting it is important first to get immediate results. This may be brought about, other factors being ruled out, by correcting the body mechanics. For this purpose it is first necessary to apply an anteroposterior pad, or, in more severe cases, an anterior pad with a light spring back-brace. It should be remembered that these children are in the rapidly growing stage, that these appliances may be quickly outgrown, and should, therefore, be frequently adjusted.

This method of treatment is purely temporary, and although it very often brings very good results, they are not permanent without properly supervised exercises to build up the weakened muscles and teach the body how to use itself efficiently.

It is necessary to follow up the application of support with muscle training, which should be persisted in for many months in order to obtain beneficial results. Since muscle training is a special field, these cases are turned over to those who are especially trained for this work.

After the application of the belt the child usually is found to have much more pep, looks better, and has better color. Very often there is no recurrence of the attacks of vomiting. On the other hand, there may be immediate improvement lasting over a period of three or four weeks, and then a relapse. It has been found that when these relapses occur the support is not properly applied, that it needs readjusting, or that the child has felt so much better that the rest periods have not been persisted in.

**Treatment of an Acute Attack.**—An acute attack may often be aborted or shortened by a free evacuation of the bowels. In my experience milk of magnesia or citrate of magnesia or calomel have been the most satisfactory. As a rule, enemata do not give satisfactory results. If the vomiting is severe, purgation should not be persisted in because the stomach usually rejects all medicines.

The child should be kept as quiet as possible in bed. The thirst may be relieved by teaspoonful doses of water every

three to five minutes. Pieces of ice placed in the mouth are often recommended, and although it gives temporary relief, it only increases the suffering when the mouth warms up. Consequently, I rarely use ice. Water ad libitum is usually rejected *in toto*, whereas small amounts given frequently often remain in the stomach long enough for absorption. Teaspoonful doses of water may be alternated with a teaspoonful of ginger ale, orange juice, or honey. Occasionally small pieces of bread or cereal without milk will be kept down, where water will not be retained. Milk is contraindicated.

After the stomach has become settled cereal jellies with sugar but without milk may be given for twenty-four to thirty-six hours. It is wise to commence with a tablespoonful every three hours and gradually increase the amount. At least thirty-six hours should elapse during which the child has not vomited before milk is given. It is then wise only to give small amounts of skimmed milk. After twenty-four hours the diet may be rapidly increased until the child is on his usual diet at the end of two or three days.

Early in an attack it is usually necessary to administer water by rectum. It is surprising how much plain water the rectum can hold in some cases. In a child of three or four years, if the water is warm, and one-half to three-quarters of an hour are taken in its administration, 6 to 8 ounces can be easily tolerated. It may be given every four to six hours. Occasionally a Murphy drip works very satisfactorily.

In my experience bicarbonate of soda usually acts as an irritant to the rectum, and should be given only as a last resort, never stronger, however, than 2 per cent.

Glucose, on the other hand, is usually well tolerated and may be introduced as a nutrition enema early in the disease in 10 per cent. solutions. In these cases it is not necessary to have chemically pure glucose. Commercial corn syrup is equally efficacious and is easily obtained.

If there is no desiccation and a true acidosis appears, the usual treatment for acidosis must be instituted.<sup>1</sup>

<sup>1</sup> This is spoken of in an earlier clinic, see Schloss, Medical Clinics of North America, 1917.

Occasionally medical treatment must be resorted to. In these instances  $\frac{1}{24}$  grain of cocaine by mouth will stop the vomiting. In other cases a hypodermic of morphine will be necessary, the dose, of course, depending upon the age of the child. If, however, preventive measures are taken and the principles outlined above are carried out conscientiously, these methods of treatment will not be necessary. Bromides and chloral usually do not effect the condition at all.

Although bicarbonate of soda in doses of  $\frac{1}{4}$  or  $\frac{1}{2}$  teaspoonful two to three times a day has been recommended between attacks on the theory that the disease is an acidosis, I do not believe that this will be found necessary if the posture is corrected and fatigue prevented.

Figure 114 is an example of a child previously reported with very poor posture. The prominent abdomen is very striking and is more pronounced below the umbilicus. The back shows a very marked lordosis. The chest is flat and the scapulae stick out behind, forming the so-called "wings." The whole attitude is one of fatigue.

It is necessary to examine these patients stripped in order to obtain a clear picture of the mechanical status of the body. Usually the cheeks of these are fat enough to give the impression of fairly good nutrition. After removing the clothes the obvious defects are a great surprise to both the parents and the physician.

Figure 115 shows the same patient after a course of muscle training. The difference in position is very striking. In the first photograph the child looks tired out, and in the second efficient and strong. The facial expression in Fig. 114 was one of fatigue, the eyes were dull, and the child did not look as if she was getting the full joy out of life. In Fig. 115 the eyes were bright and alert. The head is held erect and the sternocleidomastoid muscle has pulled up the chest so that instead of being flat it has plenty of room for expansion. The most important change is in the position of the back, which has lost its curve of weakness and shows a straight spinal column holding the weight of the body with the least possible effort. As a

result of these changes the abdomen has come into its proper position and is no longer protuberant or pendulous.

**Prognosis.**—The attacks of cyclic vomiting are often so severe that the parents fear for the outcome. Few fatalities,



Fig. 114.

Fig. 115.

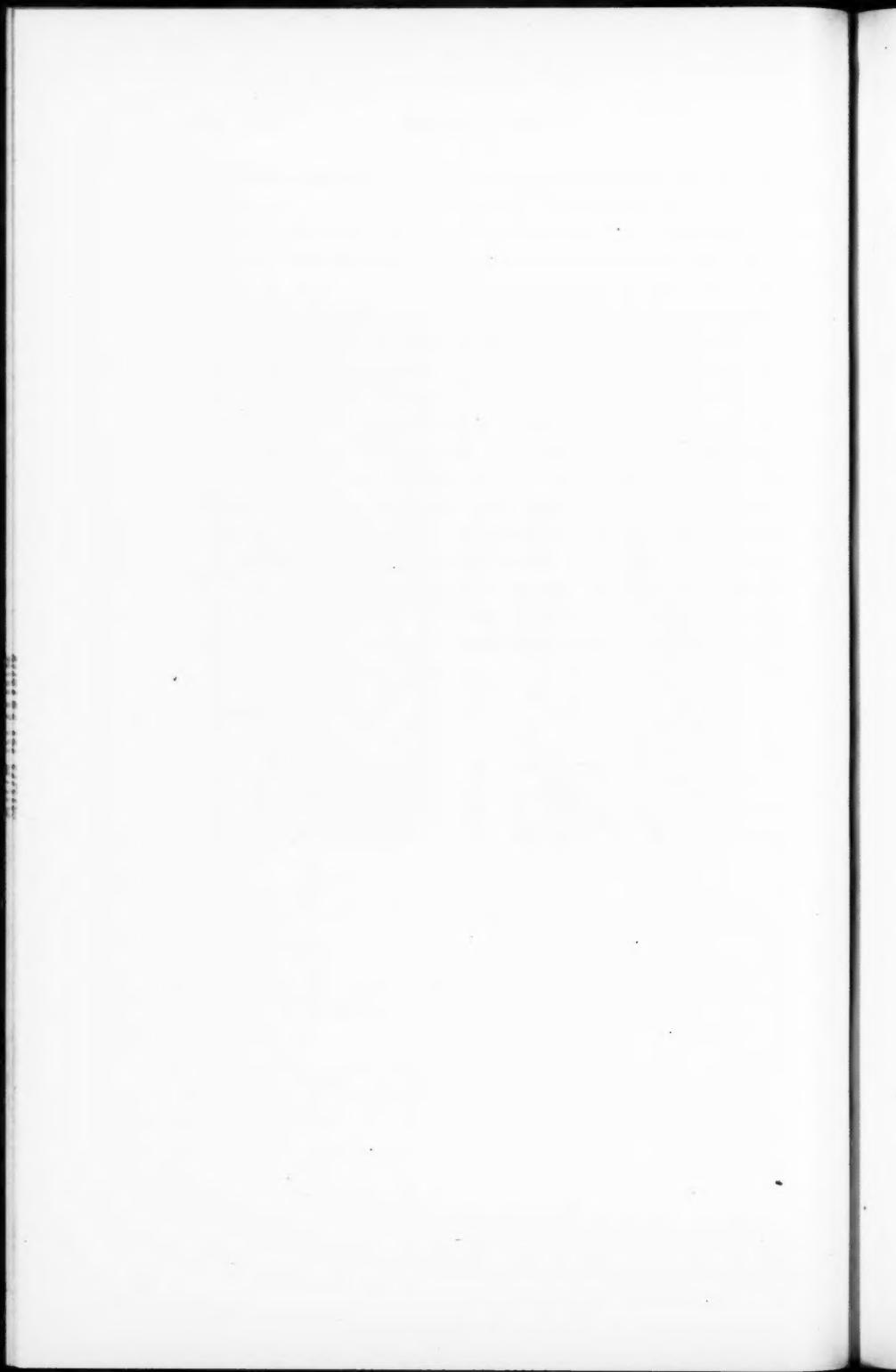
Fig. 114.—Note the characteristic appearance and poor body mechanics, especially the flat chest and the abdomen more protuberant below the umbilicus than above.

Fig. 115.—Same as Fig. 114 after postural training. Note the change in the shape of the abdomen caused by contraction of the abdominal muscles. Note also the position of the head.

however, occur in uncomplicated cases. If the body mechanics are corrected the probabilities are that the severity of the attacks will diminish immediately, and in a great many instances there will be no recurrence. The tendency to vomit, however,

may persist in some cases, and they may commence subsequent illnesses with nausea and vomiting.

**Summary.**—The conception that cyclic vomiting is due in some way to improper posture and "fractional constipation" has been the basis of treatment of cases that have come under my observation during the past five or six years. The results of treatment have been so encouraging that the correctness of this assumption seems to be justified. It seems also to show that the associated acidosis is merely a secondary symptom. There seems to be no relation between the attacks and adenoid and tonsillar infection, as shown by the frequency in which cases are not improved by a removal of adenoids and tonsils. It seems probable, then, that such infections are only accessory causes, and are only of significant importance when they are associated with poor body mechanics. Cases which do not improve with a correction of body mechanics are in nearly all instances due to a chronic appendix, even though the signs of an inflamed appendix are absent.



## CLINIC OF DR. FRANCIS M. RACKEMANN

MASSACHUSETTS GENERAL HOSPITAL

### ASTHMA

THE case of John B. brings out several important points in the diagnosis and treatment of asthma. John B. is a man twenty-two years old who has been employed in a hospital laboratory for upward of four years. His duties include the general supervision of the animal house and the handling of animals, especially rabbits and guinea-pigs. These duties take him into the animal house at least once each day, although they do not always require more than a simple inspection of the place. John has been entirely well in every way until about three months ago, when he began to notice that when he stayed in the animal room for any length of time, and especially when he worked with rabbits or guinea-pigs, he would sneeze and have itching of his eyes. Sometimes he would cough. A week or two after these first symptoms he noticed that during the evening after working with animals during the day he would have continued cough and coryza. These symptoms, however, were never severe until just before he applied for treatment in February, 1923, when for several nights he had suffered from quite severe asthma.

His physical examination was negative. He had no asthma at the time and his lungs showed no evidence of bronchitis or of pulmonary emphysema. His history was so clear cut and simple that it was not at all surprising to find a very definite skin reaction to rabbit hair and also to guinea-pig hair. This skin test was made with material prepared as follows: Some rabbit hair (and the same technic was used for guinea-pig hair) was put to soak in a solution of 20 parts of 95 per cent. alcohol in 80 parts of saline. The mixture was allowed to stand on the

desk for three days, during which it was occasionally stirred with a rod, and then it was filtered through paper to a straw colored, slightly opalescent fluid. A drop of this crude filtrate was placed on John's arm, and with a sharp glover's needle a small superficial scratch was made through it.

Figure 116 is a facsimile of the original drawing of the results of the skin tests to animal hairs and other substances as they were observed in the clinic fifteen minutes after the scratch

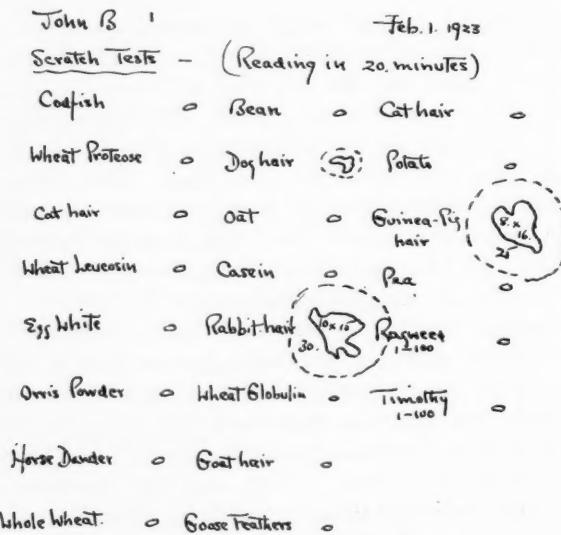


Fig. 116.—Figures show diameter in millimeters.

was made. The typical reaction as indicated consisted of a pale, sharply defined elevated area with characteristic irregular outline—a typical wheal—surrounded by a zone of bright red erythema.

From the close agreement between John's history and this skin test it became clear that John's symptoms were caused by a hypersensitiveness to guinea-pigs or to rabbits, or to both, and he was advised to avoid the animals as much as possible. Since

he could not well afford to give up his position, and since, if he continued working in the laboratory, some contact with animals was inevitable, it was determined to try to desensitize him by repeated injections of the hair extracts.

Two questions presented themselves: first, was he more sensitive to rabbits or to guinea-pigs? and second, how strong should be the first therapeutic dose? To settle these questions, the original crude filtrate was passed through a Berkefeld N. candle in order to sterilize it, and the total nitrogen was de-

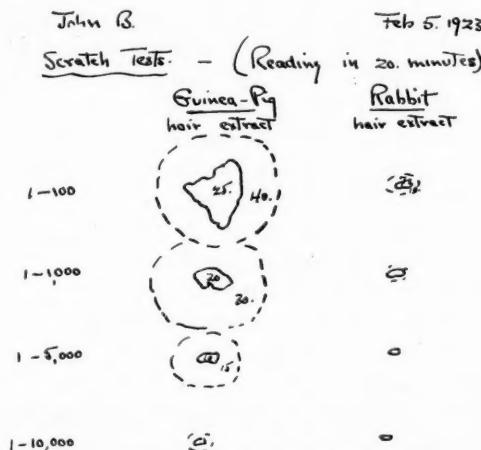


Fig. 117.—Figures show diameter in millimeters.

termined by the Kjeldahl method. The guinea-pig hair extract contained 0.4 milligram of nitrogen per cubic centimeter, while the rabbit hair extract contained 0.2 milligram of nitrogen per cubic centimeter. It is the custom in this clinic to label as 1/100 a solution which contains 0.2 milligram of total nitrogen in 1 c.c. A series of dilutions of each extract was then prepared to correspond with 1/10, 1/100, 1/000, etc.

Figure 117 shows the reactions obtained in twenty minutes by scratches made through the series of drops from each dilution as placed on John's arm. These reactions show that he was

considerably more sensitive to guinea-pig hair than he was to rabbit-hair; however, it was thought best to treat him with both extracts.

The first doses were determined by that dilution which just failed to produce a definite skin test, and were as follows:

Guinea-pig hair extract, 1/10,000, 0.05 c.c.

Rabbit hair extract, 1/1000, 0.05 c.c.

Since these first doses John has received ten doses of both the guinea-pig hair and the rabbit hair extracts. These doses were at first given twice a week, and produced reactions on his arm which appeared within a few minutes as well as swollen red areas very itchy, about the size of a 50-cent piece, and lasted for twelve to twenty-four hours. The two extracts were always given separately, the object being to keep the local reactions following inoculation distinct, so that the doses of each extract might be regulated quite independently of the other. Thus the fifth treatment was constituted as follows:

Guinea pig-hair extract, 1/500, 0.25 c.c.

Rabbit hair extract, 1/100, 0.05 c.c.

and the tenth treatment consisted of:

Guinea-pig hair extract, 1/100, 0.10 c.c.

Rabbit hair extract, 1/100, 0.10 c.c.

John's improvement began after the third dose. After the seventh dose the intervals between doses were lengthened from three or four days to seven days. After the eighth dose he went for ten days, and after the ninth dose, for two weeks. The sizes of these later doses, were, however, not increased at the same rate, as it was felt that with a longer interval the chance of producing a true anaphylactic shock would be greater. As a matter of fact, no general reaction occurred, and the local reactions following the later doses, which were so much larger than the early doses, and which were given at longer intervals, were not greater than the local reactions obtained at the start of his treatment.

At present John is well; he has no wheezing or cough at night and he can go into the animal room and handle animals without symptoms. He has, however, been careful not to re-

main in the animal room for longer than necessary. Recently he caught a cold and had a return of his wheeze at night, which improved again as his infection improved. I will refer to this again.

John's history is typical, his skin tests are typical, his diagnosis is clear, and his treatment based on this diagnosis has been easy and successful. Several points are worthy of discussion.

*First, as to Etiology.*—Here is a young man, always well, who, as far as he knows, has not had hay-fever, asthma, urticaria, or eczema, nor has he ever been susceptible to or "poisoned by" any food such as eggs, wheat, or fish. In his family is no one with asthma, hay-fever, or other allergic disease, and he remembers as far back as his grandparents.

We have been taught to compare allergy in man with experimental anaphylaxis in animals. We know that a guinea-pig becomes sensitized to some foreign protein only as a result of a previous absorption of that same protein; his sensitivity is developed to this protein alone and it is highly specific. No one has ever observed sensitiveness to any protein in a normal untreated adult animal.

In man, however, sensitiveness to some proteins may apparently develop with entire spontaneity and without any previous known contact with that protein. An infant has violent gastric symptoms when given its very first taste of egg-white; a child develops urticaria after the first meal of fish, or an adult begins without apparent reason and without change of occupation or residence to have a typical attack of hay-fever. In order to explain this it has been assumed that the "entire spontaneity" is only apparent, and that at some time and in some way active sensitization occurred in an individual who possessed a "tendency" to asthma or to hay-fever, etc. It is difficult to understand the mechanism by which sensitiveness develops. In his study of infants sensitized to egg-white Stuart<sup>1</sup> was unable to demonstrate the presence of egg-white in the breast milk of the mother. Using human breast milk obtained after feeding to the mother large doses of egg, he was unable to bring about

sensitization in normal guinea-pigs or to produce shock in pigs actively sensitized to egg-white. When, later, he deliberately added a small quantity of egg-white to human milk, his results were all positive, a fact which shows that his method was capable of demonstrating egg-white in milk when present in definite quantity. His experiments are not conclusive, however, because Rosenau and Anderson<sup>2</sup> were able to sensitize a guinea-pig with one-millionth of a cubic centimeter of horse-serum, and it is evident that any method for demonstrating the minimal quantity of egg-white necessary to sensitize must be of extraordinary delicacy. Theoretically, therefore, there is little to disprove the fact that sensitization in man as in other animals may depend upon a previous absorption of the foreign protein. In the case of the infant this protein may have entered through the placenta before birth.

Although John B. had never before had contact with rabbits or guinea-pigs, it is easy to understand that exposure to animals at frequent intervals over a period of three years finally resulted in the development of active sensitization, and from this point of view his case is important as illustrating the fact of acquired sensitization in man. It is surprising that there is no evidence of previous allergy in his own case or of allergy in his family, since we know that a "tendency" to asthma and allergy is an unknown something which is inherited according to the mendelian law (Cooke and Vander Veer<sup>3</sup>) and which occurs in the majority of sensitive cases. And this case is not the only one in which a sensitization was evidently acquired, although such a good example of acquired sensitiveness is not commonly found.

The cases of allergic rhinitis due to the orris root in face powder are becoming increasingly common. Cooke's<sup>4</sup> cases of drug idiosyncrasies are certainly of acquired origin, and the case described more recently by Larson and Bell,<sup>5</sup> of the medical student who became sensitive to urease after working with it for several months, is of the same type.

It seems fair to conclude, therefore, that sensitiveness is acquired in certain cases and may be acquired in many others.

*John's Treatment Was Successful.*—This perhaps might have been expected, but the results of treating many asthmatics who react, for example, to horse dander with an extract of the same protein, have not been good. Most of these horse-sensitive patients were sensitive to a variety of different proteins, and in most of them the association of exposure to horses with their attacks was in their minds not a close one. Most of them gave a history of attacks which were not always due to an obvious exposure to horses. Treatment with horsehair extract was given because the skin test to this protein was larger than the test to any other protein; and also because exposure to horses and to the dust of horses in the street seemed, on the whole, a more reasonable and probable explanation of their attacks than exposure to dogs, cats, or feathers, to extracts of which many of them also reacted.

In early hay-fever the patient is usually sensitive to three grasses, and there is usually some doubt as to whether to use in treatment an extract of timothy, of red top, or of orchard grass. It has been observed that whereas in one year treatment with an extract of red top was not successful, that treatment the next year with an extract of timothy did produce a good result. This would indicate that specificity is very important; that treatment must be directed toward that particular substance which causes the disease.

From these observations it seems likely that the good result in John's case was due to the fact that he was treated with a protein substance which not only caused a positive skin test, but which, in addition, represented the true cause of his asthma. This would indicate that specificity in the treatment of asthma, at least with protein extracts, is of great importance.

*Infected Asthma.*—“Recently John caught a cold and had a return of his wheezing at night.” Such an occurrence is common in asthma of almost every type. In 1918 I<sup>6</sup> described the relatively common “Complicated Pollen Asthma,” which consists simply of a bacterial infection grafted upon an underlying pollen asthma. In the same paper it was shown how one infection complicating the original asthma may be followed by

other infections each accompanied by asthma, until in a few years the asthma becomes perennial. Thus a simple uncomplicated asthma is prone to become infected and the infection is capable of changing the entire clinical picture. Per contra, it is clear that a persistent, severe asthma which lasts through the year may have had as its starting-point a sensitiveness to some foreign protein.

John's cold cleared away promptly and without incident, but other patients have not been so fortunate, and an intercurrent respiratory infection has often been the factor which changed a relatively mild disability manifest only at certain times or under certain conditions into an asthma of severe type which might occur at any time. Such an infection is common and it may be serious for this reason: during each asthmatic attack there is pulmonary emphysema of greater or less degree; the terminal alveoli are dilated while the bronchi are constricted. Since the drainage is poor, the infection can spread and may by itself cause some of the bronchial spasm. In this way a vicious cycle is soon established and the treatment of the condition becomes increasingly difficult. A knowledge of these facts should serve to emphasize the great importance of early diagnosis and of early and prompt treatment. When this vicious cycle has once become established, every effort should be made to relieve it, and the subcutaneous injection of adrenalin in doses up to 1 c.c. is by all means the best method. The action of adrenalin is to dilate the bronchi. Its administration is usually followed by the first productive cough for some hours. Adrenalin establishes drainage, and although its action is only temporary, the use of it alone is often followed by definite and gratifying results.

The case of John B. illustrates these points:

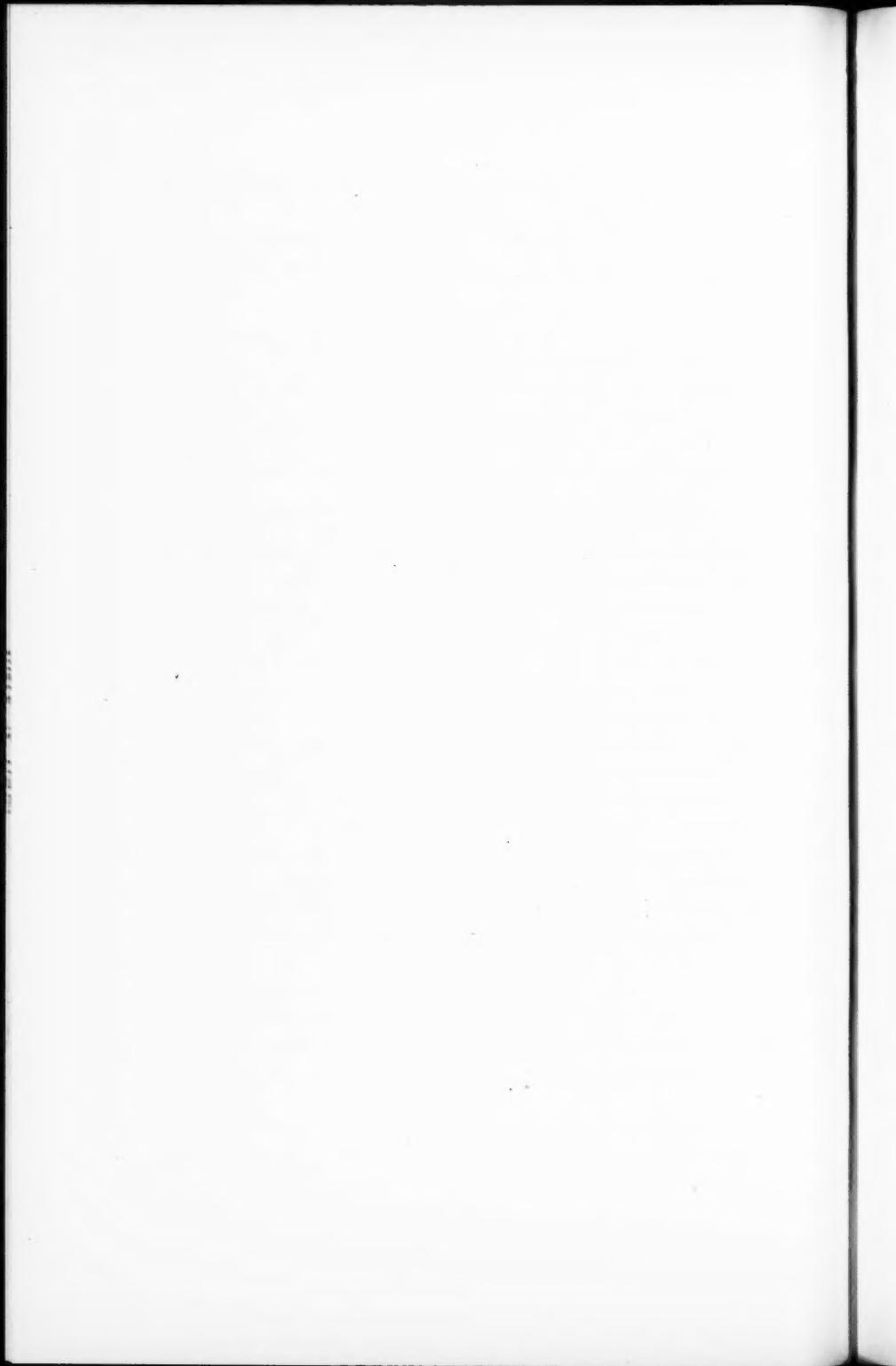
1. Susceptibility to foreign proteins may be acquired.
2. Treatment with proteins is successful according as it is specific for the particular protein substance causing the asthma.
3. Intercurrent infections in asthma are common. They are serious and they explain the progressive downward course of

the disease from a simple "spasmodic" asthma to a severe, often continuous dyspnea.

4. The danger of intercurrent infection demands the early diagnosis and treatment of the primary cause of the disease.

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CONTRIBUTION BY DR. FREDERICK T. LORD

BOSTON

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THE SERUM TREATMENT OF TYPE I PNEUMOCOCCUS  
PNEUMONIA

THIS method has now been before the medical profession for about ten years, or since Cole's<sup>1</sup> first report. It has not during that time come into general use, its application being confined for the most part to certain regions in the East.

The question may now be raised whether the time, trouble, and expense in the manufacture of the serum, the laboratory diagnosis of type, and the administration of the serum are justified by the results.

In the attempt to answer this question the steps which have led to the trial of this method may well be reviewed. The method is the direct result of laboratory studies on the pneumococcus and of experiments on animals. Such investigations have shown, contrary to previous belief, that not all pneumococci are alike in their immunologic and serologic aspects, and that out of the general group of organisms classed as pneumococci certain fixed types, known as I, II, and III, can be separated. These types are readily demonstrated by animal experiment. An animal repeatedly inoculated with sublethal doses of Types I, II, or III develops an immunity against the particular type used and not against any other type. More important still, the blood-serum of an animal thus inoculated with any one of these types possesses protective and curative action against the homologous organism, but not against any other type.

These observations led Cole and his associates to a trial of immune horse-serum in the treatment of pneumococcus pneumonia in man. It was soon observed that a sufficiently potent serum could be obtained only by the inoculation of the

<sup>1</sup> Jour. Amer. Med. Assoc., 1913, lxi, 663.

animal with Type I pneumococcus, and the serum treatment of pneumonia in man is, therefore, at present limited to the use of Type I antipneumococcus serum. The horse-serum has the disadvantage that along with its content of specific and curative antibody it contains protein substances peculiar to the horse and foreign to man, and that these may cause reactions in susceptible individuals. The experiments of Huntoon<sup>1</sup> and Cecil and Larsen<sup>2</sup> are of special interest in this connection, and it is much to be hoped that their attempt to produce a potent pneumococcus antibody unmixed with serum will prove successful.

The evidence in favor of the serum is both experimental and clinical. Regarding the experimental work investigations on monkeys are most pertinent, owing to the close phylogenetic relationship of these animals to man and their analogous response to such other specific infectious diseases as tuberculosis, smallpox, syphilis, infantile paralysis, and typhus fever. If the serum is curative for pneumonia in monkeys there can be little doubt but that it is equally effective for pneumonia in man. Of 5 serum-treated monkeys with experimental Type I pneumonia, reported by Cecil and Blake,<sup>3</sup> all recovered. These 5 animals, successfully treated, received doses varying from 0.001 to 0.3 c.c. of culture intratracheally. Two controls, untreated with serum, died following the intratracheal injection of 0.01 and 0.001 c.c. respectively. Though the number of direct controls in this experiment is small, it should be noted that one of the serum-treated monkeys received 0.1 c.c. and another 0.3 c.c. of culture, and that these amounts are one hundred and three hundred times the lethal dose, 0.001 c.c., given the control. Curative action of the serum in the treated group is further supported by their experience<sup>4</sup> in the production of Type I

<sup>1</sup> Jour. Immunology, vi, 117, March, 1921.

<sup>2</sup> Jour. Amer. Med. Assoc., July, 29, 1922.

<sup>3</sup> Studies on Experimental Pneumonia VII, Treatment of Experimental Pneumococcus Type I Pneumonia in Monkeys with Type I Antipneumococcus Serum, Jour. Exp. Med., July 1, 1920, vol. xxxii, No. 1, pp. 1-18.

<sup>4</sup> Studies on Experimental Pneumonia I Production of Pneumococcus Lobar Pneumonia in Monkeys, Jour. Exp. Med., April, 1920, vol. xxxi, No. 4, pp. 403-442.

pneumonia in 25 other monkeys of the same species. Of 5 intratracheally injected with 0.001 c.c., none recovered, and this amount would seem to be the minimal lethal dose, as all of 8 monkeys receiving more than this amount died, and all of 12 receiving less recovered. In these experiments it was noted that the earlier the serum was given, the shorter and less severe the pneumonia.

Passing now to the evidence in man, there is the report by Cole of 495 serum-treated cases of Type I pneumococcus pneumonia, with 52 deaths, a mortality of 10.5 per cent. In order to estimate the therapeutic value to the serum in these cases, however, the expected mortality without serum must be known. Of 181 collected cases (Cole, Mathers, Fussell and Famulener, Hartman and Lacy, Clough and Richardson) of Type I pneumococcus pneumonia without serum treatment, 52 died, a mortality of 28 per cent. While it must be admitted that certain desirable details in these two groups are lacking, and that the 181 cases in the control group are antecedent, not contemporaneous, yet the considerable number of cases in the two series may serve to balance possible errors.

Our series of Type I pneumococcus pneumonia treated with and without serum is as follows:

TYPE I PNEUMOCOCCUS PNEUMONIA

	Number.	Died.	Mortality, per cent.
Control group without serum.....	47 <sup>3</sup>	11	23.4
Serum on or before completion of third day.....	21	2 <sup>2</sup>	9.5
Serum after completion of third day.....	45	14	31.1
Total.....	113 <sup>1</sup>	27	23.8

<sup>1</sup> Seventy-five Massachusetts General Hospital cases and 38 seen outside the hospital.

<sup>2</sup> One of these two fatalities was a man of fifty-five treated with only 20 c.c. of serum on the third day, 160 c.c. on each of three subsequent days. The second case was a man of forty-six given four injections, beginning on

In this series it will be noted that the mortality of 31.1 per cent. in the group treated with serum after the completion of the third day of the disease somewhat exceeds the mortality of 28 per cent. in the control group without serum treatment collected from the literature. There is thus in this series no evidence that the serum is of value at this period of the disease. The mortality of 23.4 per cent. in the control group without serum is somewhat less than the expected mortality of 28 per cent. The series is, of course, too small to lay any special stress on these differences in the percentages, but it may be that a lower mortality in the control group may be ascribed to the fact that some of these cases were seen late, and seemed at the time so mild as to warrant exclusion from serum treatment. Of the 21 cases given serum on or before the completion of the third day, only 2 died, a mortality of 9.5 per cent. Although the number of cases in this group also is too small for definite conclusions, nevertheless, so far as it goes, it suggests a lowering of mortality among those treated early in the course of the disease. In connection with these 21 cases it is of interest to compare the experiences of others in Boston in similar cases. In 12 cases in Locke's series (reported at the meeting of the American Society for Clinical Investigation, Atlantic City, April 30, 1923) treated with serum on or before the termination of the third day, there were no deaths, and of 13 at the Peter Bent Brigham Hospital (personal communication from Dr. W. P. Murphy) there were 2 deaths. Altogether, then, there are 46 cases in the Boston group, treated within the first three days, with 4 deaths, a mortality of 8.6 per cent.

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the third day. In addition to the pneumonia he was found at autopsy to have hypertrophy and dilatation of the heart. There was a third death in this group, but as this patient recovered from pneumonia, to succumb following an operation for pulmonary abscess about one month later, it is included as a recovered case.

<sup>3</sup> The control group comprises cases scattered through the whole period covered by the series. Some were excluded because of a history of asthma, others because of sensitiveness to serum as determined by the intracutaneous test, others were arbitrarily recovered as controls, and still others were seen late, and recovered or died before serum could be given.

While it would be unwarranted to conclude from these figures alone that the serum is effective when given early and ineffective when given late, there is collateral evidence to support the supreme importance of early administration of anti-serum in pneumonia as well as in such other diseases as diphtheria, meningococcus meningitis, and tetanus. It is, for example, well established experimentally for pneumococcus infections that during their course substances are formed which neutralize the curative element in the serum, and it is known that these substances are formed in larger and larger amount as the infection proceeds. It is, therefore, to be expected that the earlier the serum is given, the more favorable its action will be.

A recognition of the paramount importance of early treatment with Type I antipneumococcus serum in Type I pneumococcus pneumonia naturally raises again the much discussed question of the routine use of Type I serum in all cases of pneumonia without waiting for the laboratory report of the type of pneumococcus in the pneumonia in question. But it seems undesirable to give Type I serum in this way to all cases of lobar pneumonia irrespective of type, as this would mean that about two-thirds of all patients with lobar pneumonia would be given horse-serum without any expectation of benefit whatever, and would at the same time be subjected to the discomfort of thermal and serum reactions which are likely to follow in a certain proportion of the cases.

If patients with Type I pneumococcus pneumonia are to derive the maximum benefit from serum treatment, it is clear that the diagnosis of type must be made at the earliest possible moment. There are no clinical features which serve to differentiate the types of pneumococcus infection and resort must be made to the laboratory. It is fortunate that the complex of initial symptoms in lobar pneumonia usually leaves little room for doubt as to the nature of the disease which is developing. Chill or chilliness, stitch in the side, rapid elevation of temperature, cough and expectoration, with or without blood, are sufficiently suggestive to have the sputum examined without waiting for the development of physical signs. It should by

this means be possible to complete the diagnosis of the type of infection within the first twenty-four to forty-eight hours of the onset in a very considerable proportion of the cases. It must be remembered that even after the sputum reaches the laboratory, if the diagnosis of type is made by the usual mouse method, at least eight to twelve hours and often a longer period must elapse before the tests can be completed. Even after the establishment of a Type I pneumococcus infection there is, of necessity, a still further delay of at least a few hours before the patient's sensitiveness to serum can be determined and desensitization accomplished. In one of the cases in this series the presence of a Type I infection was established by Dr. F. A. Stanwood, of Wellesley Hills, within thirty-two hours of the onset, in spite of failure to determine the type on one specimen of sputum and the necessity of repeating the tests on another. If the effort is made to determine the type of infection as soon after the onset as possible, the nature of the illness will usually be sufficiently clear by the time the typing is completed. The specimen of sputum for this purpose, from the deeper parts of the respiratory tract, should be collected in a small, clean, wide-mouthed and, preferably, sterile bottle, and should be sent at once to the laboratory. No specimen is too small for examination by the mouse test provided it comes from below. As the method of typing by mouse inoculation depends on the presence of living organisms in the specimen, no antiseptic should be added to the sputum. Bottles containing carbolic acid and in common use for the diagnosis of tuberculosis should not be used. Easily accessible laboratories open day and night should be available, and arrangements should be completed so that typing can be started at once on receipt of the specimen. It is not sufficiently appreciated that there is a rapid precipitation method of typing, described by Krumwiede and Valentine, and that if as much as 2 to 3 tea-spoonfuls of sputum can be obtained the type of infection may be determined within a few minutes.

While chief reliance in typing must usually be placed on the examination of the sputum by the mouse method, there

are other ways in which the diagnosis of type can be made. Blood-cultures obtained in all cases as early in the course of the disease as possible may lead to the establishment of the type of infection before the sputum can be obtained. By the use of Huntoon's hormone medium<sup>1</sup> we have obtained positive blood-cultures in a very much larger proportion of cases of lobar pneumonia than by the use of other media. Culture-media for this purpose may be conveniently transported in cork-stoppered bottles. Contamination in handling can be prevented by a layer of sterile cotton and several thicknesses of sterile gauze over the stopper and about the neck of the bottle. The diagnosis of type may also be made by a precipitation test with the urine of patients with lobar pneumonia. Concentration of the urine<sup>2</sup> before the application of the test somewhat increases the chance of typing by this method. Though in rare instances this method may be successful within the first twenty-four hours of the illness, it has seldom, in our hands, been of value, and then only late in the disease. The resort to lung puncture to obtain material for typing is seldom necessary if adequate effort is made by other means.

The serum treatment of Type I pneumococcus pneumonia is the direct result of laboratory experiments on animals. It is based on sound principles, and its successful application in the treatment of Type I pneumococcus pneumonia in monkeys suggests an equally important therapeutic value for man. To judge from the cases reported in the literature, there is a considerable reduction in the mortality of serum-treated cases on comparison with other cases not so treated. While our own series is still too small to admit of definite conclusions, it suggests, especially when considered with the experience of others in Boston, that the early administration of serum is of supreme importance. The results already obtained justify a continuance and wider application of the method.

<sup>1</sup> Jour. Infectious Diseases, 1918, xxiii, p. 169.

<sup>2</sup> See monograph of the Rockefeller Institute for Medical Research, No. 7, October 16, 1917, p. 30.



## CLINIC OF DR. C. W. McCLURE

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### OBSERVATIONS ON THE DIAGNOSIS OF GALL-STONES

GALL-STONES represent a common affection. At one time they were regarded as a primary condition, but gradually it has come to be recognized that the element of importance is the cholecystitis, the danger of the presence of stones being largely due to the possibility of the occlusion of the common duct by them. The mechanism of the formation of gall-stones is not altogether clear. Although their formation has been generally ascribed to the local result of gall-bladder inflammation, recent observations which have not yet been published suggest that the formation of gall-stones may be partly the result of disturbed liver function. If the cause for the formation of calculi can be established, this information may eventually allow prophylactic measures to be developed.

The majority of gall-stones can be diagnosed with considerable accuracy by clinical means and often without the aid of laboratory procedures. But, as occurs in all common affections, the condition presents itself in many bizarre forms. These forms are apt to be puzzling, and as a result the patients are referred to the gastro-intestinal clinic for diagnosis. The physicians in charge of such a clinic are supposed to have had special experience in obtaining and interpreting certain features in the patient's history, physical examination, or laboratory findings which are of great importance in diagnosis, and which are not so well recognized by one of less experience. For here, as in the vast majority of abdominal conditions, a knowledge of what findings to search for in the patient's history and laboratory examinations and how to elicit the desired findings are of

paramount importance in establishing a diagnosis. This is well illustrated in the case of a patient whose condition had been diagnosed cholecystitis with gall-stones in three of the leading clinics of America. The patient was referred to this clinic by a surgeon, who decided, after taking his own history, that the symptoms were probably not due to gall-bladder disease.

**Case I.**—The patient was a white female aged fifty-six. The essential findings of the past medical history were as follows: The patient had lobar pneumonia thirty years ago and typhoid fever twenty-eight years ago. "Nervous prostration" had occurred twenty-five years previously. A benign, cystic, lingual growth was excised one year ago. There were large varicose veins of the left leg and the corresponding ankle was occasionally edematous. There had been slight dyspnea on exertion for the past eight years. Two years ago there was a short period of night-sweats of moderate severity. The climacteric occurred ten years ago. Syphilis and other venereal diseases had apparently not occurred. There had been no appendicitis and no colicky abdominal pain, but at times severe sharp, shooting pains of momentary duration occurred in various parts of the abdomen. There had been no hematemesis, no bloody or tarry stools, and no jaundice. Nocturia occurred three or four times a night, while but little urine was voided during the day. The twenty-four-hour amount was about 2 liters.

The present illness began nine years ago, and its onset was characterized by a "terrible twisting pain under the left shoulder-blade." The pain was relieved by firm pressure on the affected region. This type of pain occurred frequently over a period of two or three weeks, and then disappeared spontaneously. Since the onset attacks of pain similar to the one described above had occurred every few months. Lying flat on the back was followed by amelioration of the pain, but on arising and exercising the pain reappeared. When the pain was unusually severe vomiting occasionally occurred; also during an attack there was much belching and mild symptoms of sour stomach.

Since the onset, nine years ago, there occurred occasionally dull aching pain under the right scapula, also sharp shooting pains in various parts of the body, especially the fingers and toes. During the past nine years the memory had been failing and the patient stated that "At times I feel weak on my feet just as though I was not sure of myself."

The findings of importance on physical examination were: (1) an enlarged pupil of the right eye (due to an injury); (2) a very moderate degree of sclerosis of the radial arteries; and (3) Heberden's nodes on the fingers. *x*-Ray examination of the organs of the chest, of the gall-bladder, kidneys, stomach and duodenum, dorsal and lumbar spines elicited nothing abnormal. The usual laboratory examinations of the urine and blood were negative. The Wassermann reaction on the blood-serum was negative.

The duodenal contents as collected and examined by the methods used in this clinic showed a color index of 5, tintometric yellow tint No. 3, and 30 mgm. of cholesterol per 100 c.c. of duodenal contents. Interpretation: Normal liver function.

In the other clinics where the patient had been studied spinal arthritis was considered as a possible cause for the pain, but it was ruled out by the negative *x*-ray findings. Cerebrospinal syphilis was ruled out because of the negative Wassermann reaction and absence of luetic history. The diagnosis of gall-bladder disease was made because of pain under the shoulder-blade and the history of dyspepsia, but there had been no other manifestations of cholecystitis.

It is conceivable that gall-stone pain could occur under the left scapula and in no other region. Nevertheless, pain in this region, even when associated with dyspepsia, is rarely due to gall-stones. Furthermore, gall-stones could scarcely account for the pains occurring in other parts of the body. For this reason further inquiries into the history of the patient were made, and the following additional information was elicited: (1) Dryness, harshness, and scaliness of the skin had been present for the past four or five years. (2) The patient did not perspire. (3) The nails of the fingers and toes had been brittle

for about five years. The hair over the vertex and ears had fallen out quite markedly for two years. (4) For the past three years the patient had fatigued easily. (5) The memory had been poor for five or six years. The ability to make decisions or to work out problems had diminished, and at times there were momentary periods of disorientation. (6) There had been marked sensitiveness to cold for three or four years. (7) The basal metabolism was between minus 24 and 27 per cent. on three examinations.

This case, then, proved to be one of myxedema, and the patient improved greatly on the administration of thyroid gland. The diagnosis was easy for any one who realized the importance of searching for special types of symptoms while eliciting a complete medical history. The improper diagnosis of gall-bladder disease was due to the lack of alertness of the various specialists whom the patient had previously consulted. Had these men been alert they would have attempted to elicit the symptoms of all diseases that could possibly cause pain of the character described by the patient. Knowledge of such conditions and of their symptomatology is of paramount importance in the diagnosis of abdominal conditions, and should always be searched for in taking a patient's history. The clue to the diagnosis in the case just discussed was the pain under the left scapula associated with pain in the extremities. This sort of pain at once suggests myxedema, as well as spinal arthritis, cerebrospinal disease, etc., as possible causes for it.

A very carefully taken history is not infrequently necessary in order to differentiate between the pain of gall-stone colic and that due to peptic ulcer. This is especially so when the patient narrates a long and confused history in which there seems to be a "complication" of diseases. In such cases one often finds that certain conventional diagnoses have been made, *i. e.*, gall-stones, chronic cholecystitis, chronic appendicitis, focal infection. In many of these cases the tonsils and other parts of the upper respiratory apparatus have been removed; and there may have been laparotomy for supposed gall-bladder or appendical disease. In the case report which follows all these

diagnoses had been made and all the operations performed except that on the gall-bladder, which the patient had refused.

**Case II.**—The patient was a nurse aged thirty-three. Influenza pneumonia, complicated with purulent otitis media, had occurred in 1921. The appendix, tonsils, and a nasal spur had been removed. Recent x-ray examination had shown no abscessed teeth. Since the age of eighteen the patient had suffered with occasional attacks of migraine, characterized by the occurrence of scintillations followed by moderately severe vertigo, and finally by severe headache, lasting about twenty-four hours. Nausea developed after the headache, but there was no vomiting. Diarrheal attacks were infrequently associated with periods of emotional strain.

For the past nine years there had occurred every few months attacks of very severe epigastric pain, which radiated through to the dorsolumbar region of the back. The pain always appeared one-half hour after a meal, and it had always been preceded by a few days of dyspeptic symptoms, which consisted of nausea and epigastric discomfort. These symptoms had led to the diagnosis of chronic appendicitis, for which an operation had been performed, without relief.

Since 1918 acute arthritic attacks would develop at irregular intervals, affecting the hips, ankles, or finger-joints. On the first consultation the knuckle of the middle finger of the right hand was considerably swollen and tender.

The amount of menstrual flow was diminished and had been almost negligible during the last three menstrual periods.

The patient stated that she "was very nervous and excitable." Her work required quick action and was a source of much emotional strain. Insomnia was another marked feature.

Except for swelling and tenderness of the knuckle-joint of the middle finger of the right hand the physical examination was essentially negative. During this and subsequent physical examinations none of the usual evidences of disturbance in internal secretion were found.

The usual clinicopathologic examinations of the blood, urine,

stools, and gastric contents showed nothing significant. Skin sensitization tests for the following proteins, found in foods commonly eaten by the patient, were all negative: Cabbage, oysters, pears, peanuts, parsnips, carrots, beets, tomatoes, onions, grape-fruit, wheat flour, mutton, peas, eggs, potatoes, oats, rice, corn, beef, milk, and pork. Basal metabolism studies repeated on two occasions were 27 and 28 per cent. below the normal.

Because of the low metabolism the patient was given 0.3 gm. thyroid extract daily. During the early part of the treatment two acute arthritic attacks occurred, each of about three days' duration. After these attacks the arthritis disappeared. During the second month of the thyroid therapy dyspepsia became more marked and was accompanied by severe nausea, and on one occasion severe epigastric pain occurred one-half hour after a noonday meal. Because of the persistent dyspepsia the gastro-intestinal tract was fluoroscoped and a marked degree of pylorospasm found. This finding, together with the character of the epigastric pain, caused the patient to be placed on a medical regimen for peptic ulcer. On this treatment the symptoms quickly disappeared.

The above patient's case report presents four classes of symptoms, as follows: 1, A functional group, the so-called neurotic type, comprised of headaches, nausea, malaise, lassitude, and diarrheal attacks associated with emotional strain. 2, Chronic arthritis with acute exacerbations. 3, Amenorrhea. 4, Epigastric pain.

The patient had done about as much as possible to correct psychologic and working conditions which could affect the neurotic symptoms. The presence of arthritis and amenorrhea suggested, among various possibilities, an endocrine disturbance. For this reason the basal metabolism was determined and was found to be much below the average normal. This indicated hypofunction of the thyroid gland, and afforded a rational basis for the administration of extract of thyroid. Under this treatment the acute exacerbations of arthritis disappeared, the amenorrhea became less marked, and the neu-

rotic train of symptoms grew less severe. But the epigastric pain occasionally occurred, as it had in the past, and there was much nausea without vomiting.

Until the effect of the thyroid therapy was established, no special therapy was directed to the gastro-intestinal tract, in order that the part played by the administration of the thyroid extract in the relief of symptoms might be ascertained. However, the administration of thyroid did not affect the epigastric pain or nausea. The question then arose as to the possible correctness of the previous diagnosis of gall-stones, since the history of the character and the *x*-ray finding of localized spasm in the stomach might very well have resulted from gall-stones, among other causes, for the two most common causes for epigastric pain are gall-bladder disease and peptic ulcer. Other somewhat less frequent causes are cerebrospinal disease, renal colic, colonic conditions, pancreatitis, angina pectoris, spinal arthritis, and rarely food protein sensitizations. Chronic appendicitis is often stated to be another cause. But experience leads me to believe that chronic appendicitis is an uncommon cause for epigastric pain. Occasionally one observes pain limited to the epigastrium in the presence of renal calculi or colonic disease. But the history of these two conditions is so different from that of cholecystitis and peptic ulcer that confusion in the differential diagnosis is rare. Furthermore, proper *x*-ray studies will practically settle the question of diseased kidneys and may aid in the diagnosis of colitis. The differential diagnosis from mild recurrent attacks of acute pancreatitis is most difficult, for the reason that the diagnosis of pancreatitis is so difficult. If the recurrent attacks are the result of a chronically diseased pancreas, the laboratory aids may furnish tell-tale evidence of it. These consist of the determination of the patient's sugar tolerance, including the blood-sugar curve, of the presence of steatorrhea, and of the estimation of the enzymic concentration of the duodenal contents. If these determinations show nothing abnormal, one is usually forced to disregard the rôle possibly played by the pancreas. In the case under discussion the tests and procedures discussed were all made and nothing abnormal

was found. The cardiovascular system was essentially normal and x-ray examinations showed nothing abnormal in the spine. There being no other evidences of cerebrospinal disease than the epigastric pain, a lumbar puncture was not done; that source of trouble seemed very unlikely in this particular patient. The skin tests for food proteins were all negative. The findings, therefore, largely ruled out the usual causes for epigastric pain except for the two commonest ones, *i. e.*, gall-stones and peptic ulcer.

What help does the history give in the above case in differentiating between the pain of peptic ulcer and that due to gall-stone colic? The salient feature in the history is that the pain always occurred one-half hour after meals. This time relation between the onset of the pain and the ingestion of food is highly suggestive of the presence of peptic ulcer. The next feature of importance to be considered is that of the x-ray findings. Fluoroscopy showed persistent pylorospasm. Persistent pylorospasm may be associated with many abdominal lesions, and especially with gall-bladder disease. But in the case under discussion the pylorospasm was associated with a definite time relation of the pain to the ingestion of food. The association of these two symptoms makes the diagnosis of peptic ulcer highly probable. Under medical treatment for peptic ulcer the patient became free from symptoms.

The 2 cases reported and discussed clearly and forcefully demonstrate the value of history study in obtaining a clue to the diagnosis, and how x-ray and other laboratory aids may frequently be of great assistance in establishing a diagnosis suspected from the findings obtained in the history. The cases, also, demonstrate how experience in a certain branch of medicine gives the physician an acumen which cannot be gained in any other way. However, they show most emphatically that the physician in a clinic which confines its work to abdominal diseases must be always on the alert for medical conditions which are not primarily abdominal.

While the history is usually the decisive factor in the diagnosis of gall-stones, there is a group of icteric cases in which

this is frequently not so. In this group the difficulty lies in differentiating between obstruction of the common bile-duct due to gall-stones and that due to malignancy. When jaundice is due to malignancy the three most frequent sites of the cancer are in the head of the pancreas, in the bile-ducts, and in the liver as secondary to cancer of the stomach. In making the differential diagnosis between secondary hepatic cancer the *x*-ray is often decisive, since cancer of the stomach as the primary lesion is almost always demonstrable by *x*-ray.

In this group gall-stones may be suspected from the history if it shows the occurrence of recurrent attacks simulating gall-stone colic, if there have been recurrent attacks of "nervous dyspepsia" for a year or more, if there have been recurrent attacks of jaundice, or if the jaundice present has definitely varied in intensity from time to time. But these features are often not obtainable in the history. When this is the case and when the physical examination and *x*-ray studies elicit nothing of decisive diagnostic import, then the diagnosis becomes problematic. Under these conditions the proper examinations of duodenal contents frequently elicit information of great aid in establishing the true pathologic condition present. For this reason it is considered important that the physician understand the purposes and the technic of obtaining duodenal contents and their examination.

Duodenal contents are examined for evidences of normal or abnormal functioning of the liver and the pancreas, and are obtained by means of the duodenal tube. The duodenal tube is familiar to all. It is swallowed by the patient after a fasting period which has been sufficiently long to insure that the stomach contains no food. The tip of the tube is allowed to pass through the pyloric sphincter and into the second portion of the duodenum, which position of the tube is ascertained by aid of the fluoroscope. The patient then reclines on the right side.

To obtain duodenal contents for examination of bile 50 c.c. of 33 per cent. solution of Epson salts is instilled into the duodenum through the tube. The proximal end of the tube is then closed by a pinch-cock for five minutes, after which pe-

riod the contents are allowed to siphon off until they become distinctly yellow in color. As soon as the yellow color appears, the contents are caught in a clean, dry flask, and are thus collected over a period of thirty minutes. These duodenal contents are then examined for color, for bile-pigment concentration, and for the concentrations of cholesterol and bile acids.

The method used for the determination of the cholesterol concentration has been published, but those for the other determinations have not. For this reason a short description of them will be given. The color is determined by means of a tintometer. The tintometer consists of a series of unchangeable colored solutions prepared from inorganic salts. By means of this tintometer the bile of duodenal contents collected under abnormal conditions has been found to differ from that of normal contents in intensity or shade of color, or both. Bile-pigment concentration is estimated by comparing the depth of the yellow color produced in duodenal contents by a method to be described elsewhere, with a set of arbitrary standards. The technic of this method is a very simple one; as is, also, the tintometric method for establishing the color of duodenal contents described above. The method for determining the concentration of bile acids is about as simple as a quantitative method using a Duboscq colorimeter can be made; the method depends on the color reaction between bile acids and furfural.

Besides the chemical tests the biliary fraction of duodenal contents is examined microscopically for a large excess of cholesterol and for calcium bilirubin crystals.

To obtain duodenal contents for examination of the pancreatic secretion the duodenal tube is given in the manner described. The patient then drinks a mixture consisting of 40 c.c. of 20 per cent. cream (ordinary heavy cream) in which is suspended 15 grams of barium sulphate. The barium is added because it has been found that cream often appears in the duodenal contents more quickly when mixed with barium than when given alone. After ingesting the cream and barium mixture the patient lies on the right side, and the flow of duodenal contents is initiated by gentle suction with a syringe. As soon as

the flow is started, the duodenal contents are allowed to siphon off, and are collected for one hour after barium first appears in the collection flask.

Enzymic concentration is determined by estimating the activities of the proteolytic, lipolytic, and amyloytic enzymes of duodenal contents, which are active in alkaline media. The methods used are those devised by McClure, Wetmore, and Reynolds; and the determinations are made within eighteen hours after collecting the duodenal contents. How much longer than eighteen hours the enzyme's remain stable has not been determined. Proteolytic activity is estimated by allowing a dilution of the duodenal contents to act on a solution of casein. The casein not affected by proteolytic action is precipitated by means of metaphosphoric acid solution. The index of proteolytic concentration is taken as the number of milligrams of nitrogen not precipitated by the metaphosphoric acid. This nitrogen value is determined by an adaptation of the method of Folin and Wu for the determination of non-protein nitrogen in the blood. Amylolytic activity is estimated by the number of milligrams of glucose developed by action of duodenal contents on a solution of soluble starch. The index of amylolytic concentration is taken as the total number of milligrams of glucose developed, as determined by the method of Folin and Wu for the determination of sugar in the blood. Lipolytic activity is estimated by allowing duodenal contents to act on a true emulsion of cottonseed oil, and determining the amount of acidity developed by titrating with tenth-normal solution of NaOH in alcohol. The total number of cubic centimeters of N/10 NaOH necessary to neutralize the acidity developed is used as the index of lipolytic concentration. The samples of duodenal contents and the reagents used must be controlled for the presence of nitrogen not precipitated by metaphosphoric acid, for copper-reducing bodies and acidity. In a certain number of cases it will be found that the duodenal contents obtained both from patients and from normal subjects are so viscid that pipeting is difficult. The results obtained, however, in examining such specimens are entirely comparable to those obtained in

cases in which the viscosity is not excessive. The extremely viscid duodenal contents are diluted as called for by the method for estimating amylolytic activity and filtered through dry filter-paper. With this precaution the final blue solution is not turbid.

The aid obtained from the use of the laboratory procedures described in differentiating between benign and malignant causes for jaundice will be illustrated by a small series of case reports. The first case demonstrates the value of normal enzymic concentrations of duodenal contents in excluding cancer of the head of the pancreas.

**Case III.**—The patient was a female aged sixty-one. The preoperative diagnosis was cancer of the head of the pancreas and the postoperative diagnosis was chronic cholecystitis with stone in the common duct.

The patient had been jaundiced one and a half years before the present attack. Fourteen months prior to the present illness the left breast had been removed because of a non-malignant growth about 10 cm. in diameter. The present attack of jaundice was first noticed four weeks before admission to the hospital, and was associated with anorexia, nausea, epigastric distress, and some loss in weight. On physical examination the patient showed deep icterus, the liver edge was indefinitely felt 2 cm. below the right costal margin, and the ascending colon was palpable.

Roentgen examination showed gastric hyperperistalsis and the second portion of the duodenum was moderately dilated.

The patient was under observation three weeks before laparotomy was done. During this time the jaundice remained unchanged, but all food was vomited during the first two weeks. After that period vomiting became much less pronounced. The liver edge became definitely palpable 4 cm. below the right costal border and there developed a small, firm, non-tender, egg-shaped mass just below the edge of the liver in the mid-clavicular line.

Duodenal contents derived from the cream meal were white in color. Enzymic concentrations were as follows: proteo-

lytic 2.9 mgm. non-protein nitrogen; lipolytic 2.8 c.c. of N/10 NaOH; and amyloytic 3.1 mgm. glucose. Duodenal contents derived from the instillation of magnesium sulphate contained no bile-pigment. These findings were interpreted as showing normal pancreatic function and complete obstruction of the common bile-duct.

Except for bile in the urine and the fatty stools usual in obstructive jaundice, the clinicopathologic laboratory findings were essentially negative.

On laparotomy a large calculus was found in the ampulla of Vater. There was, however, no distention of the common bile-duct, which did not contain bile. The gall-bladder was greatly distended, but the contained fluid was not bile colored. Following laparotomy the patient recovered and remained well.

There is a point in the history of this case (Case III) which is suggestive of gall-stones as the cause of the jaundice, and that is the story of a slight attack of jaundice one year previous to the present one. However, the attack was slight so that the surgeons questioned the actual presence of it. Their opinion was that the present attack of jaundice was the result of cancer of the head of the pancreas, and it was only with great difficulty that a surgeon could be induced to operate. But there was one laboratory finding which largely ruled out malignant involvement of the head of the pancreas. This was the finding of normal enzymic concentrations of duodenal contents. There were then two probable diagnoses, *i. e.*, malignancy of the bile-ducts or stone impacted in the common duct. The absence of bile from the duodenal contents might have resulted from either stone or cancerous obstruction of the common duct. Nevertheless, bile is more often absent from duodenal contents in the presence of malignancy than of gall-stones. So that its absence suggested malignancy. Repeated lavage of the duodenum might have produced a flow of bile, and this would have largely ruled out cancerous obstruction, as will be discussed later. However, this was not done. Another feature suggestive of cancer was the history of the removal of a tumor from the breast, in spite of the fact that histologic examination showed it to be

of benign character.  $\alpha$ -Rays of the gastro-intestinal tract were negative. Thus the findings narrowed the diagnosis to either stone or cancer of the common duct. The fact that there was a history of jaundice one year previous to the present attack, associated with the findings tending to rule out metastasis from the breast or from the stomach, and to rule out cancer of the pancreas was more indicative of the presence of gall-stones than of cancer. On laparotomy, occlusion of the common duct by a stone, located above the ampulla of Vater, was found.

In this case (Case III)\* mention was made of the rôle in diagnosis of the presence or absence of bile-pigment in duodenal contents. An initial absence of bile-pigment from duodenal contents followed by its presence after repeated lavage of the duodenum with magnesium sulphate solution is of much importance in diagnosis, as is illustrated in the following case report.

**Case IV.**—The patient was a white female aged fifty-three. The diagnosis was cholecystitis with gall-stones. Two years before admission to the hospital there had been an attack characterized by dull epigastric pain, some vomiting, and much weakness. This attack lasted one week. Eight months before admission the patient had been studied on the surgical service of the Peter Bent Brigham Hospital. At that time she had been jaundiced for six weeks and had complained of much dull epigastric pain, located in the right portion. The jaundice remained for nearly three months, and then gradually disappeared. During the next five months the patient was free from symptoms except for transitory, mild epigastric pain. The patient then became jaundiced again and entered the hospital. On admission physical examination showed the patient to be fairly deeply jaundiced and somewhat emaciated. The liver edge was palpable 3 cm. below the right costal margin; the surface was smooth.

Hemoglobin was 75 per cent., white blood-cells, 11,200 per cubic millimeter, and the red cells 4,800,000. The smear was not unusual. The urine contained bile and occasionally sugar.

The stools were gray in color and microscopically showed large amounts of fatty acids (patient on a low fat diet). The duodenal contents at first contained no bile, but after the use of magnesium sulphate lavage on a few occasions bile reappeared.

On laparotomy the gall-bladder contained many stones and a stone was found in the ampulla of Vater. The gall-bladder and ducts were markedly thickened.

In this case (Case IV) it will be noted that the initial absence of bile from the duodenal contents was associated with abnormally low enzymic concentrations and that the return of the presence of bile was accompanied by increase of these concentrations to normal. These findings are explained by a lessening of the degree of obstruction in the ampulla of Vater. Thus the initial absence of bile and low enzymic concentrations followed by a return of bile and the increase to normal of enzymic concentrations indicates a benign obstruction to the common duct.

What lesion may be expected when repeated lavage of the duodenum with magnesium sulphate fails to produce a flow of bile is illustrated by the following case.

**Case V.**—The patient was a male negro aged fifty-six. The diagnosis was carcinoma of the head of the pancreas involving the common bile-duct. The present illness began six weeks prior to admission to the hospital. During the first two weeks there were gaseous eructations and bloating of the epigastrium, and epigastric distress at night, relieved by soda or hot water. The taking of food caused dull aching in the epigastrium beginning five to ten minutes after eating and lasting from three to twelve hours. Jaundice developed four weeks prior to admission to the hospital, and was accompanied by pruritus and profuse sweats. Lying on the right side caused nausea. Slight dyspnea had been present since the onset.

On physical examination the scleræ and skin were deeply jaundiced. The liver edge was palpable 5 cm. below the right costal margin; it was firm and its surface irregular. There was moderate tenderness in the epigastrium, more particularly

just to the right of the midline. There was right inguinal hernia.

Fluoroscopic examination demonstrated a concave defect in the outline of the lesser curvature side of the antrum and first portion of the duodenum. This finding suggested pressure from without the gastro-intestinal tract. The duodenum was lavaged with magnesium sulphate solution on several occasions, but the duodenal contents were always free from bile-pigment. The enzymic concentrations were, proteolytic 1 mgm., amylo-lytic 0, and lipolytic 0. These findings showed complete obstruction to the common duct and marked obstruction to the pancreatic duct.

Hemoglobin was 88 per cent., white cells 9000, and red cells 4,000,000 per cubic millimeter. The blood-smear was not unusual. Wassermann reaction on the blood-serum was negative. Gastric analysis showed a moderately low free HCl and total acidity. Benzidine test was negative in both gastric contents and stools. The findings in the urine and stools were those usual in obstructive jaundice.

On laparotomy, a large adenocarcinoma of the head of the pancreas, and involving the common bile-duct, was found.

Thus the above case shows that in cancer of the head of the pancreas of sufficient size to cause jaundice bile-pigment is absent from the duodenal contents, and that the enzymic concentrations remain low in spite of lavage with magnesium sulphate.

Repeated lavage with magnesium sulphate may fail to produce the presence of bile, while the enzymic concentrations are normal throughout. What lesion may be expected in the presence of this set of findings is illustrated in the following case report.

**Case VI.**—The patient was a white woman aged forty-seven. Five years ago there had been a breast operation for a small malignant growth. Four months ago a gall-bladder excision had been done for chronic cholecystitis. The present illness began as jaundice, without pain or vomiting. The physical

examination showed a thin, nervous woman, deeply jaundiced. Other than for the scars of the previous operations and the jaundice the physical examination was essentially negative.

*x*-Ray studies showed the following: Plates of the gall-bladder and kidneys demonstrate no signs of disease. A barium meal gives the picture of a small horizontal stomach toward the right. The stomach outline is normal. The first and second portions of the duodenum are dilated and show marked stenosis. The whole duodenum takes a wider curve than usual, as if there was some body pressing on the inside, such as an enlarged head of the pancreas.

Laboratory examinations of the urine and stools gave findings usual in obstructive jaundice. Duodenal tube in second part of duodenum and 33 per cent. magnesium sulphate instilled produced white duodenal contents. The enzymic concentrations of the duodenal contents were: proteolytic 3 mgm., lipolytic 2.1 c.c., and amylolytic 2.6 mgm. Repeated lavage of duodenum with magnesium sulphate solution for the next three days failed to produce bile in the duodenal contents.

On laparotomy, carcinoma obstructing the common bile-duct, but not involving the pancreas, was found.

In this case (Case VI) the presence of normal duodenal enzymic concentrations and the negative *x*-ray findings in the stomach largely rule out cancer of the pancreas or stomach as causes for the jaundice. The persistent absence of bile-pigment from the duodenal contents after repeated lavage with magnesium sulphate was highly suggestive of malignancy involving the common duct. However, this finding will occasionally occur when the obstruction is due to gall-stones, and this prevents it from being of diagnostic import. But in the case under discussion the persistent absence of bile together with the history of breast cancer made the diagnosis of cancer highly probable, and cancer of the bile-duct was found at laparotomy.

Besides the findings in duodenal contents which have been discussed there are others concerning the biliary and pancreatic fractions of duodenal contents which are of importance in the diagnosis of gall-stones. One of these findings consists of di-

minished concentration of bile-pigment, associated with normal concentration of the enzymes of duodenal contents. This is illustrated in the following case report.

**Case VII.**—The patient was a white female aged fifty-nine. The preoperative diagnosis was cancer of the head of the pancreas and the postoperative diagnosis was stone in the ampulla of Vater. The present illness had begun four weeks prior to admission to the hospital. The earliest symptoms had been those of moderately severe dyspepsia, followed in a few days with jaundice of the skin and sclerae. There had been no abdominal pain.

On physical examination the patient was seen to be deeply jaundiced. Her mentality was considerably dulled. The liver edge was palpable 3 cm. below the right costal margin. Its edge was rounded and its surface smooth.

The usual clinical examinations of the blood, including the Wassermann reaction, were negative. The urine and stools were those usual in obstructive jaundice. Duodenal contents after lavage with magnesium sulphate contained a small amount of bile-pigment. Contents derived from the cream meal showed enzymic concentrations of normal degree (proteolytic 2.7, lipolytic 1.6, amylolytic 1).

At laparotomy, a stone obstructing the common duct and located in the ampulla of Vater was found.

A preoperative diagnosis of gall-stones in this case was made by the medical service. This was based solely on the findings of some bile-pigment and normal enzymic concentrations of the duodenal contents. No clue to this diagnosis was obtainable from the history. The latter was rendered unreliable by the patient's mental condition.

Occasionally examination of the duodenal contents, obtained from a jaundiced patient, shows diminution in the concentration of enzymes and the presence of bile-pigment in decreased amount. In such a case diminished enzymic concentration could be the result of either cancer of the head of the pancreas or of gall-stones obstructing the ampulla of Vater; but

cancer of the head of the pancreas sufficiently large to cause jaundice has so far been found to completely occlude the common bile-duct and thus exclude bile from the duodenum. So that the findings of bile in duodenal contents, in the presence of diminished enzymic concentration, is very suggestive of benign obstruction of the common bile-duct, and this is illustrated in the following case report.

**Case VIII.**—The patient was a white female, aged fifty-five. The surgeon's preoperative diagnosis was cancer of the head of the pancreas, while the postoperative diagnosis was gallstones occluding the ampulla of Vater. The past medical history elicited a story of severe colicky pain of an hour's duration and located in the right lower quadrant, occurring three years prior to the present illness. During this period of three years there had been attacks of dyspepsia at irregular intervals and characterized by epigastric burning, some water-brash, moderate nausea, and discomfort after meals.

The present illness had been present four months at the time this history was taken. The onset was with dyspepsia, *i. e.*, moderate nausea, vomiting after meals on a few occasions, epigastric discomfort, and anorexia. These symptoms were soon followed by jaundice. There had been no pain. Two months after the onset the dyspeptic symptoms disappeared. The patient was sure that there had been periods of a few days in which the skin had been less yellow in color and the urine of lighter color. There had been "considerable" loss in weight, but the patient ate little food.

Other than for deep icterus the physical examination was essentially negative.

Hemoglobin was 80 per cent., white blood-cells 10,000, and red cells 4,800,000 per cubic centimeter. Wassermann reaction on the blood-serum was negative. The stools and urine were as usual in obstructive jaundice. Duodenal contents obtained after the instillation of magnesium sulphate shows an abnormally small amount of bile-pigment. Contents derived from a cream meal showed abnormally low enzymic concentrations

(proteolytic 1 mgm.; lipolytic 0.2 c.c., and amylolytic 0.2 mgm.).

On laparotomy, the ampulla of Vater was found obstructed by a gall-stone and there were no evidences of malignancy.

There is one other finding in duodenal contents which has proved of aid in differentiating benign from malignant cause for jaundice. This finding is the presence of sufficient amount of blood to tinge the duodenal contents a decided red color. When this amount of blood occurs in the absence of bile and abnormally low enzyme concentrations of the duodenal contents, the presence of cancer involving the head of the pancreas, the common duct, and the duodenal wall is highly probable.

## CLINIC OF DR. JOSEPH H. PRATT

BOSTON

### SOME COMMON ERRORS IN THE DIAGNOSIS OF HEART DISEASE\*

FOUR cases are to be shown, and from each a lesson of importance can be learned. I present them because they emphasize so strikingly the necessity of considering the possibility that a patient with symptoms or signs suggestive of disease of the heart may have a perfectly healthy heart. If the subject of symptoms apparently directly referable to the heart or circulation be a young adult the chances are that the heart is sound. The physicians who knew most about heart disease in the armies of the Allies and of Germany and Austria during the World War all agreed that a great majority of the cases sent to the hospitals with a diagnosis of organic heart disease had no disease of the heart. Systolic murmurs of no significance were regarded as evidence of valvular disease, and on rapid heart action of psychic origin was often based the mistaken diagnosis of myocarditis or a weak heart. The error of the first examining physician who mistook a trivial disorder of cardiac function for organic heart disease often left in the patient's mind the idea that his heart was seriously diseased so firmly fixed that it remained for months in spite of the assurance of abler physicians that his heart was sound. Self-observation of the heart's action with apprehension increased the symptoms in thousands of cases.

Here we have four ex-soldiers from the wards of this hospital taken almost at random from the group of cases in which a diagnosis of organic disease of the heart or aorta has been made. In one case some doubt has been expressed as to the existence of valvular disease, and Dr. Barlow, who some months ago

\* Clinic given at Veterans Bureau Hospital No. 41, New Haven, Conn., March 23, 1923, in the School for Instruction of Physicians of the Bureau.

made the diagnosis of aortic insufficiency in the case, asked me to examine the patient. Now this case, as I shall attempt to show, is the only one of the four in which a definite diagnosis of organic heart disease can be made. The other three, if we use the diagnostic standards of the present day, must be regarded as having healthy hearts.

The first patient is a native of the Philippines, aged twenty-eight. Last September he developed a cough and was admitted with the diagnosis of pulmonary tuberculosis. Tubercl bacilli have not been demonstrated in the sputum. The physical signs in the lungs are indefinite, and Dr. K. Dunham, who examined the radiograms last week, said they were not characteristic of tuberculosis. Dr. Barlow thinks he has a non-tuberculous infection of the lungs, and I agree with him.

A tentative diagnosis of syphilitic aortitis has been made in this case by one of the physicians. It was thought as a result of the x-ray examination that the aorta was dilated. The Wassermann test was a "four plus" positive. The x-ray finding of a dilatation of the ascending aorta we must reject, as the picture was taken with the tube close to the patient. This gives a distorted and enlarged shadow of the heart and the aorta. A teleradiogram should be made, that is, a plate taken with the cathode at a distance of 2 meters from the patient. It would be well also to make a fluoroscopic examination at this distance in what is technically called the "first oblique diameter," as this gives a view of the anterior and posterior borders of the aorta and of the space between the aorta and the vertebral column. An aortitis causes such a marked change in the shape and size of the aortic shadow seen in the oblique diameter, that is, from the left posterior part of the chest to the right anterior, that it is easily recognized. Beware, however, of making diagnosis of aortitis from x-ray evidence alone. I saw a number of cases ten years or more ago when that diagnosis was based largely on an increase in width of the shadow of the aorta in ordinary anteroposterior radiograms. None of these cases that was followed developed clinical evidence of this disease.

One should distinguish between aneurysm and aortitis. Practically all cases of saccular aneurysm are due to syphilitic aortitis, but in only a relatively small percentage of the cases of aortitis does an aneurysm form. In Romberg's<sup>1</sup> series of 220 cases of syphilitic aortitis only 16 per cent. developed an aneurysm. Syphilitic aortitis is often overlooked during life. This is not due to the absence of clinical evidence, but to the failure to recognize that the symptoms are caused by an aortitis. The predominating symptoms in many cases are due to myocardial insufficiency, aortic insufficiency, or angina pectoris. The chief subjective symptom is pain over the upper sternum. This man has had no pain in the chest. Breathlessness on slight exertion is usually present in aortitis as a result of myocardial involvement, and this symptom is also absent in our patient.

In aortitis there is generally found on inspection of the chest a pulsation in the episternal notch and, in addition, in the second or first interspace on one or both sides of the sternum. There is dulness over the manubrium. This is important. On auscultation the second aortic sound often has a ringing bell-like quality which is characteristic of this disease. T. McCrae<sup>2</sup> has given an admirable description of the clinical features of aortitis which if generally known would lead to the more frequent recognition of a disease that has received too little attention in this country. In this patient before us none of the physical signs mentioned are present. Furthermore, the age of the patient makes syphilitic aortitis rather improbable. He is only twenty-eight years old, and both aortitis and aneurysm are unusual in one so young. The average age at which aortitis occurred in a large series observed by Romberg was forty-nine years. It is the latest of all the visceral manifestations of syphilis. Hubert<sup>3</sup> found the average interval between infection and the development of symptoms to be twenty-three years. The disease, however, may occur in young individuals, and Longcope,<sup>4</sup> in his thorough study of syphilitic aortitis, had an unusually large number under thirty years of age. The average latent period, however, in his series was sixteen years.

Dr. Connor<sup>5</sup> has called attention to the rarity of aortic

aneurysm in the army examinations during the World War. Among 1,000,000 examinations of drafted recruits in the United States there were 11,562 rejections for cardiovascular disorders. But only 20 of these were for thoracic aneurysm. On the basis of these statistics he was justified in emphasizing his conclusion that "in cases of acquired syphilis the clinical evidences of involvement of the aorta and heart almost never appear before the thirty-fifth year." Dr. Connor has told me recently that he is now convinced that aneurysm is somewhat less rare in early life than the army diagnoses indicate. Dr. Longcope's study shows that the disease does occur before the thirty-fifth year in a considerable number of persons, although doubtless it is much less frequent than his experience would indicate. Thirty-two, or 50 per cent., of his 63 cases in which the diagnosis was confirmed at autopsy were between the age of twenty and forty. The conclusion however, seems evident that many cases of syphilitic aortitis must have been overlooked by the army examiners.

In the case under consideration I feel sure that the diagnosis of syphilitic aortitis can be dismissed.

The second case I will show you has been diagnosed mitral insufficiency of valvular origin. There is no history of rheumatic fever. The cardiac impulse cannot be felt and the percussion outline of the heart is normal. There is a systolic murmur at the mitral area, but it is distinctly audible only when the patient is recumbent. It is heard with maximum intensity over the pulmonary area. Now the diagnosis of mitral insufficiency is quite unjustified in this case. It has been based solely on the presence of the systolic murmur. There is no other evidence. Systolic murmurs at the apex or over the pulmonary area are present in many men with healthy hearts. Cohn<sup>6</sup> examined with care 214 soldiers who had done hard service overseas, and found murmurs in 109 instances, or 50 per cent. In 68 the murmur was heard in the recumbent position only. In the circular of instructions<sup>7</sup> for examination of the heart and blood-vessels of recruits issued by the Surgeon-General's Office in the summer of 1917 the following statement occurs: "It cannot be too strongly

insisted on that, given a heart of normal size and responding normally to effort, any murmur that is heard should be considered accidental and insignificant unless it can be positively demonstrated that it is a mitral or aortic diastolic murmur." Many physicians still look upon mitral insufficiency as of common occurrence and easy to recognize. Instead of being the easiest valvular lesion to diagnose it is often the most difficult. This is clearly brought out by the third patient I shall demonstrate to you. This man served three months in the navy. He had no difficulty in doing his work and was never short of breath on exertion. The diagnosis of mitral insufficiency was then made, and he was discharged. He was later in the army doing limited service, and had no symptoms of heart weakness. About a year ago he became ill and was admitted to this hospital with pulmonary tuberculosis. Now a loud systolic murmur is present in this patient and it largely replaces the first sound and is well transmitted to the axilla. If the diagnosis could be made on the murmur alone then there would be no doubt that this man has mitral insufficiency, as the murmur is loud and does not differ in any way from that heard in endocarditis of the mitral valve with insufficiency. But, as I have said, the best authorities at the present time agree that a systolic murmur no matter how loud or well transmitted to other areas of the chest does not justify the diagnosis without evidence of cardiac hypertrophy or dilatation, or a definite history of rheumatic fever. There is no history of rheumatic fever. The sign of cardiac hypertrophy is a heaving impulse. You will note that there is a fairly wide area of visible and palpable impulse in the fourth and fifth interspaces, but it is not heaving, that is, it is not very forcible. The outward thrust can be easily overcome by the pressure of my fingers. It is visible over a wider area and more forcible than when I examined him in the ward. The temporary increase in the force and rate of the heart action is evidently due to natural excitement or nervousness due to this demonstration before a large group of physicians. The impulse can be felt just outside the nipple line in the fourth interspace, but in the fifth interspace it is not outside the nipple line. This

is not clear-cut evidence of cardiac enlargement. The maximum impulse is inside the nipple line. This man at the present time has a diffusion of the cardiac impulse. This was common in soldiers, at least in the British Army, who had no dilatation of the heart, although sometimes it spread from the third to the seventh interspace (Lewis<sup>8</sup>). If this man had a forcible impulse in the fourth space outside the nipple line when the heart action was slow, I should regard that as evidence of cardiac enlargement. The percussion outline is not definitely increased. This radiogram was taken with the tube close to the patient. The heart shadow is magnified. It does not measure in width 50 per cent. of the width of the chest wall. If the plate had been with the patient 2 meters from the cathode and the heart shadow was then less than half the width of the chest, we could say positively that the heart was not enlarged. A teleradiogram yields a silhouette that is the exact size of the heart in the coronal plane. It gives the true width and length of the heart, but not the anteroposterior diameter. The measurements of the silhouette should be made in the various conjugates and compared with the standard tables for normal men made by Dietlen<sup>9</sup> or Otten.<sup>10</sup>

Hypertrophy or dilatation cannot be shown to exist on physical examination. A teleradiogram giving measurements above the normal is necessary in the case before the diagnosis of mitral insufficiency is justified. Two of the three criteria of mitral insufficiency are requisite for a diagnosis: (1) A systolic murmur at the apex, (2) a history of rheumatic fever, (3) hypertrophy or dilatation of the heart. Rothschild<sup>11</sup> found that among 870 recruits with systolic murmurs accepted for limited service in the army only 33, or 3.8 per cent., had either one of the two other criteria for the diagnosis of mitral insufficiency. This shows how wide-spread is the false idea that a systolic murmur is evidence of mitral insufficiency. This point must be emphasized as strongly as possible. Sir James Mackenzie<sup>12</sup> impressed it upon the British examiners early in the war, but in three months, he tells us, it was forgotten and systolic murmurs were again looked upon as a sufficient cause for rejection from

the army. Lewis<sup>13</sup> says: "Medical men generally do not or cannot differentiate between a systolic murmur which is and which is not significant. Many believe they can. More men have been discharged wrongly from the army (or have been overassessed) on account of these signs than because of any other presented by the cardiovascular system."

Here are two men with the diagnosis of mitral insufficiency. The first has certainly a normal heart, and in the second the diagnosis is doubtful. A systolic murmur when detected should make one examine the heart with especial care. That is, one should note whether there is hypertrophy or dilatation. Inspection, palpation, and percussion should be employed with attention to every detail. The murmur of early mitral stenosis should be sought, and searching inquiry made regarding the previous occurrence of rheumatic fever. From my own experience I have learned that even a loud systolic murmur may lack any significance. Let me cite one case: Mrs. F. M. S. in 1896 consulted her family doctor for palpitation of the heart. He discovered a systolic murmur and made a diagnosis of heart disease. She was thirty-four years old then. In 1912, when I first saw her, she said walking rapidly did not produce breathlessness. She had never had rheumatic fever or chorea. The three physicians she had consulted in the previous sixteen years all agreed she had valvular disease of the heart, and one of these was an able Boston consultant. I wrote at the time of my first examination the following note on the heart: "At the beginning of the examination the patient was excited. The pulse-rate was rapid and the cardiac action forcible, but not heaving. When the patient was erect the apex-beat was felt 8 cm. from the midline in the fifth interspace. In the recumbent position the apex impulse was located in the fourth interspace just inside the nipple line. There is no dulness to the right of the sternum. Absolute cardiac dulness begins 1.5 cm. to the left of the median line and is 7 cm. wide. Its upper border is at the level of the fourth costal cartilage. No systolic murmur is audible at the mitral area, but when recumbent a systolic murmur can be heard accompanying a loud first sound. Passing

upward along the left sternal border the murmur increases in intensity and is very loud at the pulmonary area. There is no definite accentuation of the pulmonary second sound. Pulse 100 to the minute, regular in force and rhythm. Peripheral arteries not sclerosed."

I wrote the physician who referred the patient to me the following comment: "This is a very interesting case. The symptoms are evidently of nervous origin. There is no sign of cardiac hypertrophy. This is strong evidence against mitral insufficiency. Balfour's statement, quoted by Osler (*Practice of Medicine*, 6th ed., p. 813), should be borne in mind, that the pulmonary area is the region of romance. There is no history of rheumatism. It would be of value to have an examination made with the orthodiograph in order to determine the exact size of the heart. The patient states, however, that she is satisfied with the correctness of my opinion and is unwilling to make another visit to Boston for a confirmatory examination."

Seven years later (1919) I was again called to see the same patient. Ten weeks before I saw her a consulting physician, and a man whose opinion I usually value highly, had decided that a cough that had persisted for a year was due to heart failure. The blood-pressure was found to be 180 mm. of Hg. He instituted strict bed-rest and a nurse was installed. The pulse, which averaged about 72 for the first three weeks of bed treatment, became more rapid after she was allowed to be up for four or five days. On this account she was put back to bed. She was "absolutely exhausted" the first day after resuming strict rest. On inquiry I found that up to the time that heart failure had been diagnosed she had done all her own cooking, and this exertion had produced no shortness of breath. For three weeks before I saw her she had been low spirited. She felt she would not recover. She was much disturbed when her pulse was a little rapid, that is, when the rate was 90. She often asked her husband to feel her pulse. She was preoccupied with her own condition.

On examination, aside from a pulse-rate of 140, I found no

change in the condition of the heart from that noted in 1912. The lungs were normal. The cough had ceased in a couple of weeks after she had been put to bed. I felt convinced it was of hysterical origin. "The apex impulse is felt in the fourth interspace 8 cm. from the median line, when recumbent 9.5 cm. It is not increased in force. Right border of relative cardiac dulness is 2 cm. to the right of the median line. Left border of relative cardiac dulness is 10 cm. to the left of the median line. Absolute cardiac dulness begins in the median line and is 9 cm. wide. Upper border of absolute cardiac dulness is in the fourth left interspace. . . . A high-pitched systolic murmur accompanies the first sound at the apex. The second aortic and second pulmonic are not accentuated. Radial arteries are not sclerosed; systolic blood-pressure 180, diastolic 78; second determination 174, third reading 176, and diastolic 78. The patient's expression was anxious. She was evidently much depressed. She asked me early in the examination if I thought she had any chance of recovering. She added that she knew the rapid pulse was a very bad sign. I made the same diagnosis as I had seven years before—Neurasthenia; accidental cardiac murmur. I wrote in the record the following comment: "No signs of cardiac weakness. If cough were due to weakness of the heart, there would be other signs present, such as dyspnea or râles at the bases of the lungs, if my experience is a trustworthy guide." I advised the patient to leave her bed and if possible to go away and to try to enjoy herself. I noted on my record that "confinement to bed is increasing her apprehension and introspection."

Five weeks later her physician wrote that "the patient made an uninterrupted recovery and has discharged the nurse and also her doctor and rides about in her auto wherever she likes." I have just learned (March, 1923) that the patient has had no further symptoms referable to her heart and has remained in good health.

This case I have presented in detail because the record covers a space of twenty-seven years, from 1896 to 1923, and because it answers a question so often asked: "What is the

future history of the cases with definite systolic murmurs at the apex with no other signs of cardiac disease and no history of rheumatic infection? Here at least is the history of one patient who was told in 1896, at the age of thirty-four, that she had heart disease because a systolic murmur was discovered, but who at sixty-one still presents no evidence of cardiac weakness. I have reported the case for another reason, and it is this: If four physicians of more than average ability, two of them teachers of medical students, based a diagnosis of mitral insufficiency on a systolic murmur alone, there must be a great many others even at the present time who do not use sufficient caution in making this diagnosis. Osler used to tell us in our student days that we should not make the diagnosis of aortic stenosis until we had a few gray hairs. Possibly it might be well to extend the application of this rule to mitral insufficiency, but, unfortunately, we all know that age does not always bring wisdom.

Now to return to the patient I have just shown you, the third on the list. Let us assume that he has a chronic endocarditis producing mitral insufficiency, and that the teleradiogram at 2 meters will show definite enlargement of the heart. What is the prognosis? Sir James Mackenzie tells somewhere in his writings of his surprise when he heard Graham Steele, of Manchester, make the statement that patients do not die of mitral insufficiency. Twenty-five or more years later Mackenzie wrote that he had never seen a fatal case of mitral insufficiency since his attention was called to the benign nature of this lesion. He referred to pure mitral insufficiency. When cases do badly there has always been in my experience a mitral stenosis present in addition to the insufficiency. Even when the cardiac enlargement is marked the cardiac power may be fairly well preserved. I saw on October 21, 1913 G. W., a woman then twenty-six years of age. She gave a history of rheumatic fever at the age of twelve and a second attack at seventeen. The heart was involved and a physician of distinction told her father that she would not live to be twenty years old. When I saw her there was a wide area of visible cardiac impulse. On palpa-

tion a heaving impulse and systolic thrill were felt at the mitral area. The left border of pulsation extended into the axilla. A long, loud, rough, systolic murmur was heard over the cardiac area with maximum intensity at the mitral area. It was transmitted over the entire chest. There was no dulness to the right of the sternum. The left border of cardiac dulness was near the midaxillary line. She complained of "pounding of the heart and skipping of the pulse" on exertion. She was not breathless on exertion. In October, 1918 her vital capacity was 2500 c.c., which was 81 per cent. of her normal for her weight and height according to West's standard.<sup>14</sup> I have tested many women with healthy hearts whose vital capacity was no more than this. I saw her this spring (1923), and her general condition is better than it was in 1913, and the response of her heart to effort has not lessened in this period of ten years. [On June 1, 1923 her vital capacity was 2850 c.c.]

Before dismissing the subject of mitral insufficiency attention should be called to the importance of listening carefully for a diastolic murmur at the mitral area in every case in which a systolic murmur is present, in fact, in every case in which the suspicion of cardiac disease exists. The diastolic murmur of beginning mitral stenosis easily escapes detection. As mitral stenosis is such a serious disease, it is most important to recognize its existence. The murmur may not be audible except immediately after exertion. Morison<sup>15</sup> has found that inhaling an amyl nitrite pearl may enable one to hear a murmur that could not be detected otherwise. In all doubtful cases special means of increasing the heart rate, either exercise or inhaling amyl nitrite, should be used to bring out the murmur, and the patient's mitral area carefully auscultated before the heart rate falls to the former level.

The fourth case for demonstration was the only one in which the diagnosis of organic disease of the heart or aorta was questioned. Curiously enough, it turns out to be the only one of the four in which the diagnosis of organic disease is undoubted. Dr. Barlow asked me to examine the patient because a few months ago he made a diagnosis of aortic insufficiency, but a physician

who examined the heart more recently reported that nothing abnormal was found. Dr. Lewis A. Connor,<sup>5</sup> in his excellent paper on the lessons in cardiac diagnosis learned from the army physical examinations, says that "aortic insufficiency was the one valvular lesion in which the tendency to err was in the direction of making the diagnosis too infrequently." The diastolic murmur when faint and high pitched was occasionally overlooked. Our present case supports Connor's statement. The man has not had shortness of breath on exertion. There is no pulsation visible in the peripheral arteries. The pulse is not collapsing, the systolic blood-pressure is not elevated. The cardiac impulse is in the normal position and is not increased in force. The percussion outline is normal. There is, however, a faint but distinct blowing diastolic murmur in the third and fourth left interspace near the sternum. It is louder in the recumbent than in the erect posture. The diagnosis of aortic insufficiency can be made on this physical sign alone and with a feeling of assurance in its correctness. But in the present case the diagnosis is strongly supported by the patient's past history. While serving with the army in France he had a severe attack of rheumatic fever. It is now known that rheumatic fever and its ally, chorea, which is probably simply a different manifestation of the same infectious agent, are the cause of nearly all the cases of aortic insufficiency and mitral stenosis in young persons. In view of a definite history of rheumatic infection in this man even a systolic murmur should not be lightly regarded, and an early diastolic murmur along the left sternal border, even in the absence of all other signs of cardiac disease, makes assurance doubly sure that this is a case of aortic insufficiency.

I hoped that I could discuss with you the subject of the cardiac neuroses, but lack of time forbids anything more than a brief reference to this important topic. Some patients under emotional stress and strain exhibit neuromuscular, gastric, genital, respiratory, or cardiac symptoms. Why one person when mentally agitated should feel distress over the heart and another should have an attack of diarrhea is an unsolved prob-

lem. From the time of Homer and probably earlier it has been known that strong emotion affected the action of the heart. Galen tells of his discovery of the exact cause of a lady's illness which he had previously suspected was of mental origin from the fact that the pulse became rapid and irregular whenever the name of a certain actor, Pylades, was mentioned, and at no other time. He rightly concluded that she was love sick.

Most of the cases with heart symptoms that developed among the soldiers were suffering not from any disease of the heart, but from a psychoneurosis in which the physical reaction to strong emotion, usually fear, affected the heart rather than the neuromuscular system or the gastro-intestinal tract. As a matter of fact, the neuromuscular system as well as the heart was affected in most of the cases of so-called soldier's heart or effort syndrome.

Among 1000 cases of D. A. H. (disordered action of the heart) studied by Hume<sup>16</sup> among British soldiers, 76.8 per cent. had pain in the chest, 67.5 per cent. breathlessness, and nearly 100 per cent. complained of exhaustion. On the other hand, practically all the soldiers who were sent to the special hospitals for psychoneurotic cases were found to have some complaints referable to the cardiovascular system. Burton-Fanning,<sup>17</sup> who had a hospital for neurasthenic cases that developed among the soldiers of the home forces in England, said that pain below the cardiac region was a very frequent complaint and that the majority of his 500 neurasthenic soldiers complained of dyspnea. They had a pulse-rate of 100 or more.

The term "effort syndrome" proposed by Lewis is not very satisfactory because it implies that effort is the cause. Later studies made by Oppenheimer and Rothschild,<sup>18</sup> Robey and Boas,<sup>20</sup> Campbell,<sup>21</sup> Cohn,<sup>6</sup> and others showed clearly that the effort syndrome, or the irritable heart of soldiers, was a form of the war neurosis. It was not effort or infection or heart strain that caused it, but emotion. It resulted from a faulty adaptation of the individual to his environment and the struggle to accept the life situation in which he was placed. Emotion got the upper hand of reason and the abnormal mental state

developed to which the term "neurasthenia" is applied. The emotive cause in the war was usually fear. Its evil effects were often seen in those who were constitutionally predisposed even in the early weeks of training. The symptoms of the so-called effort syndrome were present in many cases before the recruits had been subjected to any great effort or had been ill with any infection. Fear in various forms—fear of death, fear of sickness, fear of failure, fear of punishment, acted on many of those temperamentally unfitted for the life of a soldier from the time they left their homes for the training camps. The instinct of self-preservation dominated their emotional life and the physical symptoms which developed can be reasonably explained on the theory of a defense reaction which had as its purpose preservation of the individual from the dangers of war. Morbid mental processes set up by fear awakened suppressed tendencies connected with the instinct of self-preservation, an instinct more fundamental and more concerned with the production of neuroses than the sexual instinct (Rivers<sup>21</sup>).

A study of the cardiac neuroses during the war revealed the fact that in many soldiers the symptoms had been present, but less marked before they entered the army. The cardiac neuroses in civil life differ only in degree not in kind from the typical cases of the soldier's heart so well described by DaCosta,<sup>22</sup> Lewis,<sup>8</sup> and Cohn.<sup>6</sup>

The percentage of cases with cardiac symptoms that are of psychic origin is much less in civil practice than it was in the army during the war. In a group of 637 soldiers of the British Expeditionary Force with cardiac symptoms or signs analyzed by Lewis, 516, or 81 per cent., were diagnosed as effort syndrome. These according to present teaching would now be classed as cases of cardiac neurosis. Romberg<sup>24</sup> says that neuroses of the heart or vessels comprise about 25 per cent. of the patients who consult him for disturbances of the heart or circulation. I have analyzed 250 cases with cardiac symptoms seen in my private practice, and found the percentage much lower. Only 30, or 12 per cent., of my group were cardiac neuroses, but the percentage in young patients, that is, in those under thirty

years of age, was much higher than this. I think my percentage is unusually low. Gerhardt<sup>26</sup> had 109 neuroses, 38 per cent., in his series of 289 patients with heart symptoms seen in consultation practice.

It is not enough to assure the patient with cardiac symptoms of psychic origin that his heart is normal. In the majority of cases this is quite ineffectual. Thoroughness in diagnosis and success in treatment demand that the cause of his mental maladjustment be brought to light. Take the case of the first patient I showed. You noted his anxious expression. He told me that he sleeps poorly; his appetite is gone, and he has indigestion. He also complains of constant pain above the left costal border, but below the heart. He does not believe he has pulmonary tuberculosis now, but is in constant fear he will contract the disease before he is discharged from this hospital. As the decision has been reached that he has had a non-tuberculous infection of the lungs, and if my opinion is confirmed that he has a normal heart and aorta he probably will recover from his present symptoms soon after he is discharged from the hospital, especially if he finds congenial work.

In the diagnosis of heart disease consider not physical signs alone or signs combined with symptoms, or with the response of the heart to exercise, for these are not sufficient, but consider the whole man, body and soul together.

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CLINIC OF DR. CHESTER M. JONES

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**SOME SERIOUS ASPECTS OF INFECTIOUS (CATARRHAL)  
JAUNDICE**

THE unusual prevalence of epidemics of jaundice during the past few years has led to an increased interest in a study of the epidemiology and pathology of the disease. There exists at present, however, a very unsatisfactory state of confusion throughout the literature regarding the classification of this disease, variously referred to as epidemic catarrhal jaundice, infectious jaundice, epidemic jaundice, etc. Further confusion is added in classifying those scattered cases commonly known as catarrhal jaundice. A recent epidemiologic study by Blumer<sup>1</sup> of the various outbreaks of jaundice throughout the country has contributed considerable information and aids in a more satisfactory understanding of the subject. Blumer believes the various epidemics, although of no proved etiology, to be infectious in origin, but not due to spirochetal infection. He further believes that cases of so-called catarrhal jaundice may be sporadic cases of the epidemic form. Recent work done at the Massachusetts General Hospital by Jones and Minot<sup>2</sup> helps to confirm the infectious nature of the disease, and the identity of the epidemic and endemic form. Observations on a large number of both types of jaundice led to the conclusion that the entire group of cases is best included under the term "infectious jaundice." Clinically, both types were identical. The onset and course of symptoms were the same in each. Physical examination in cases of so-called catarrhal jaundice and in epidemic jaundice practically always revealed a palpable, tender liver, and frequently a palpable spleen. The duration of the jaundice varied within similar limits in each. Slight elevation of tem-

perature occurred at the onset of the attack in both forms. Examination of the duodenal contents at the onset of the disease always revealed a sediment consisting of large numbers of bile-stained leukocytes and biliary tract epithelium—evidence of a definite inflammatory process. Furthermore, there was observed a fact not previously reported, namely, that in all typical cases there exists a characteristic blood-picture, which is present in both the epidemic and the sporadic form. A slight initial leukocytosis, with a subsequent leukopenia, associated with an absolute rise in the lymphocytes and large mononuclears, was found in all but the very atypical cases. This increase of the lymphocytes and mononuclears was accompanied by a striking vacuolization of the latter. These vacuolated mononuclear cells were thought to be phagocytic endothelial cells, probably derived from the liver and the spleen.

It has seemed entirely logical, therefore, to classify all the cases previously known as catarrhal jaundice, epidemic jaundice, etc., under the single heading of infectious jaundice. This disease should be sharply differentiated from "Weil's disease," which is best classified as spirochetal jaundice.

It is the purpose of this communication to emphasize the possibility of unusually severe reactions and of serious complications occurring during the course of an attack of infectious jaundice. The usual course of the disease is characterized by certain well-known clinical manifestations. Ordinarily the disease is ushered in by an acute onset of malaise, anorexia, and gastro-intestinal disturbance, followed shortly by the appearance of jaundice, with dark urine and clay-colored stools. As already noted, the liver is nearly always enlarged and tender, and the spleen is frequently palpable. The duration of the jaundice varies within rather wide limits, but in mild cases it usually extends over a period of from two to three weeks, while in the more severe cases icterus may persist for three or even more months. Pruritus is often a distressing symptom, and there may be a rapid loss of weight. Complications are rare, and convalescence is usually uneventful. I should first like to emphasize, however, several important points in a consideration

of the usual cases of infectious jaundice. A prolonged course is not at all uncommon, and in any but the younger patients may be very disturbing. Jaundice persisting over a month in an elderly person quite logically makes the diagnosis of infectious jaundice somewhat difficult to maintain unless all other possibilities have been completely excluded. Roentgen-ray examination of the gastro-intestinal tract and gall-bladder region, a careful analysis of the duodenal contents, and treatment by duodenal lavage can usually establish the diagnosis. Even in well-established cases, however, the loss of strength and weight may be very disturbing, and may render a convalescence of several months a necessity. Several cases, recently seen, have lost over 30 pounds in weight, with a corresponding loss in strength. Careful dietary measures are obviously necessary to bring about a return to normal. In all cases, however, a slight anemia is developed, and in the more severe cases a drop of almost 2,000,000 red cells per cubic millimeter has been frequently seen. Recovery from such a grade of anemia is a gradual one, covering a period of many weeks.

A further point of importance for a proper understanding of the disease is the fact that there is a striking delay between the first rapid improvement in the intensity of the jaundice and its final disappearance. This delay in the disappearance of clinical icterus frequently covers a period of a month or more. It is due to a continuation of the toxic process in the liver parenchyma—a fact that is not generally appreciated. The proof for such a statement lies beyond the scope of this paper, but has been adequately covered in another communication.<sup>2</sup> This toxic phase of the jaundice is entirely analogous to the jaundice associated with diarsenol poisoning, tetrachlorethane poisoning, and the like. It would seem highly probable that this toxic phase, if severe enough, might account for the rare cases of infectious jaundice that suddenly progress into acute yellow atrophy.

A further point of importance is the not infrequent occurrence of exacerbations of the jaundice during convalescence. Such relapses have occurred in several of our cases in both the

mild and severe form. They are characterized by a deepening in the intensity of the icterus, and by a return of malaise and mild gastro-intestinal disturbances. These exacerbations, except in the most severe cases, last for a few days only. In certain cases, however, they may occur just as the jaundice has nearly disappeared, and may then persist for several weeks or more. In 2 cases the relapse was more severe than the original attack, persisted for nearly two months, and caused grave fears for the ultimate prognosis.

It is of interest to note that in all cases except those associated with rare complications there is little or no elevation of temperature.

In view of the above considerations I believe the most intelligent method of following the progress of any case of infectious jaundice should include certain measures. These should consist of frequent examinations of the duodenal contents, including bile-pigment estimations, repeated determinations of the serum bilirubin, and a study of the changes in the white count and differential count. A dropping serum dilution, associated with a continuous rise in the duodenal bile-pigments, a leukopenia, and an early increase in the lymphocytic and mononuclear elements of the blood are all good prognostic points.

I shall now turn from a general consideration of the disease to a discussion of certain unusual features of infectious jaundice. Although not definitely proved to be direct complications of infectious jaundice, these exceptional features have been seen with sufficient frequency in otherwise typical cases to warrant their inclusion in this discussion. These complications or sequelæ are, indeed, of great practical importance, and have not received sufficient attention in the literature. That the liver is involved in all cases of infectious jaundice is becoming more and more widely recognized, but the possibility of serious chronic liver pathology seems to have been largely overlooked. I shall report 4 cases seen at the Massachusetts General Hospital during the past year which fall clearly into the group of infectious jaundice, but which, contrary to the usual course, went on to a serious termination.

**Case I.**—H. T. G. (E. M. 255,042), male, aged twenty-six.  
*Past History.*—Unimportant.

*Present Illness.*—The onset of the disease occurred one year prior to admission to the hospital. It began with the usual symptoms of an upper respiratory tract infection—malaise, coryza, headache, anorexia. These symptoms continued for two weeks without relief, at the end of which time he felt very weak and first noted jaundice. At the same time he noticed that his urine was dark and his stools clay colored. In addition, he had symptoms of indigestion, with belching, nausea, and epigastric distress. There was no vomiting or acute abdominal pain. Symptoms were most marked a half-hour to an hour after meals. The jaundice gradually deepened, and persisted, with variations in intensity for several months. There was marked loss of weight and strength, and pruritus was a distressing feature. It is of importance to note that the case occurred in the midst of an epidemic of jaundice (New Haven, Conn.), and was similar in its initial stages to the other cases in the same locality. After seven months, during which the jaundice persisted with varying degrees of intensity, the patient was sent to a surgeon, who advised operation. The preoperative diagnosis was said to be chronic cholecystitis. Laparotomy was performed, the gall-bladder was removed, and drainage was established by means of a biliary fistula. Following the operation the patient drained bile for two months, with a diminution in the intensity of his jaundice, and with constant clay-colored stools. At the end of this period a second operation was performed, anastomosing the biliary fistula with the duodenum. Convalescence was uneventful, and surgically the operation was successful. Since that time, however, the patient has continued to be slightly jaundiced at intervals. The stools and urine were said to be normal following the second operation. It seems reasonable, therefore, to assume that the operation may have been responsible for at least part of the clinical improvement.

Following the second operation the patient's appetite improved and there was some gain in weight. Any exertion com-

pletely exhausted him, however, and he slept very poorly. On admission to the hospital one year after the onset of his jaundice his presenting symptoms were marked weakness and loss of weight.

*Physical Examination.*—The patient showed on physical examination pallor, slight icterus of the scleræ, emaciation and muscular weakness, abdominal scars from two operations, and a palpable liver. The liver edge could be felt about 2 cm. below the costal margin, was firm and smooth, and was not tender. The spleen was not felt. The examination was otherwise negative.

*Laboratory Findings.*—Urine and stools normal. Red count: 4,800,000 cells per cubic millimeter. White count: 7800 cells per cubic millimeter. Hemoglobin (Tallqvist) 75 per cent. Differential count: polynuclear neutrophils, 72 per cent.; polynuclear basophils, 1 per cent.; large mononuclears, 9 per cent.; lymphocytes, 18 per cent. Stained blood-smear showed some achromia of the red cells and some anisocytosis. The platelets were normal. Fragility of the red cells in varying concentrations of salt solution: hemolysis began at 0.42, complete at 0.32. Wassermann negative. Serum dilution 1 : 30 (Gmelin test on serum positive).  $\alpha$ -Rays of the gastro-intestinal tract were negative.

*Course.*—While in the hospital the patient had few complaints except for general weakness, fatigue, and anorexia. The jaundice varied from day to day, at times being imperceptible, and at other times showing in the scleræ. There was no associated rise in temperature or pulse with these fluctuations in the jaundice, and there were no variations in the symptoms. The patient was discharged unrelieved, with the diagnosis of cirrhosis of the liver. It seems probable that the case will progress gradually to a fatal termination, with increasing anemia, cirrhosis, and its allied complications.

**Case II.**—A. W. C. (W. M. 255,607), female, aged fifteen.

*Past History.*—Unimportant. Always in good health.

*Present Illness.*—Fourteen months prior to admission to the

Massachusetts General Hospital the patient had an acute upper respiratory tract infection, with fever, malaise, headache, sore throat, anorexia, and mild gastro-intestinal symptoms. There was no abdominal pain. Following the acute onset she developed jaundice with dark urine and clay-colored stools. Pruritus was marked and the headache and anorexia persisted. Intense jaundice lasted for several weeks, with the concomitant signs of biliary obstruction. Several days following the onset of the disease in this patient her younger sister also became jaundiced, but entirely recovered within three weeks. There was at the time an epidemic of jaundice in the same locality (Bridgewater, Mass.). After several weeks of intense jaundice, with associated loss of strength and weight, the elder sister's condition gradually improved, with a diminution in the depth of the icterus. The latter did not disappear, however, but remained to a very slight degree. Five months after the original attack the patient began to suffer from epigastric distress after meals. This was followed by nausea and vomiting. The vomitus consisted of partly digested food and bile. These symptoms persisted until admission to the hospital. Throughout the summer, fall, and winter the icterus persisted, with the occasional appearance of dark urine and light colored stools. A month prior to admission there was a mild respiratory infection, associated with an abrupt exacerbation of the jaundice. This persisted for a week, with an increase in all the symptoms, and then for a second time the jaundice returned to only moderate intensity. On admission the chief symptoms were intense weakness, a striking distaste for food, and nausea and vomiting. There was some epigastric distress following an attack of vomiting. The patient had lost 35 pounds in weight since the onset of the disease.

*Physical Examination.*—An emaciated, sallow, tired-looking young girl, with slight icterus of the skin and scleræ. The liver edge was palpable and slightly tender. The spleen was not felt. The lower pole of the right kidney was just palpable. The pulse was slow (60) and of fair quality. There were no other abnormal findings.

*Laboratory Findings.*—Urine: negative on five occasions; bile in very small amounts on two occasions. Stools: dark brown; guaiac negative. Red count: 4,260,000 cells per cubic millimeter. White count: 9600, 8200, 7200, 8800, 6000 cells per cubic millimeter. Hemoglobin (Tallqvist): 85 per cent (admission); 70 per cent. (discharge). Differential count (admission): polynuclear neutrophils, 70 per cent.; large mononuclears, 4 per cent.; lymphocytes, 26 per cent. Other differential counts showed a reduction of the polynuclear cells, with an absolute rise in number of lymphocytes. A count toward the end of the stay in the hospital showed: polynuclear neutrophils, 39 per cent.; large mononuclears, 6 per cent.; lymphocytes, 55 per cent. The stained smear showed achromia of the red corpuscles, moderate anisocytosis and poikilocytosis, and irregularity in filling of the red cells with hemoglobin. The platelets were slightly increased. Wassermann negative. Fragility of the red cells in varying concentrations of salt solution: hemolysis began at 0.48, complete 0.38. Clotting time, twenty-eight minutes; with calcium chlorid, twelve minutes. Bleeding time, two and a half minutes. Serum dilutions: 1:120, 1:75, 1:100, 1:50, 1:35, 1:150. (These observations were taken at intervals during a month's stay in the hospital.) Liver function test (phenoltetrachlorphthalein): admission, 7 per cent. of dye retained in blood-stream after one hour; discharge, 14 per cent. of dye retained at end of one hour.  $\alpha$ -Rays of gastro-intestinal tract and gall-bladder region negative. Gastric analysis negative, except for hypo-acidity.

*Course.*—From an examination of the laboratory data it can be seen that there was a definite secondary anemia, a jaundice of varying intensity as measured by the serum dilutions, and a marked inability of the liver to properly excrete a specific dye. The clotting time was abnormal, due undoubtedly to an alteration in liver function. While on the ward the patient's condition fluctuated greatly. The jaundice persisted throughout, but varied as already noted. Following frequent duodenal washings the jaundice decreased and the symptoms improved somewhat. The appetite returned to some extent, and the

vomiting ceased for a time. There was a continuous loss of weight, however, and toward the end of a month the patient could be said to have improved but little. The temperature was always normal, but the pulse was slow, and at times there was a true bradycardia, with a rate of 45 to 50. At times the patient was very drowsy. The duodenal contents always showed an abnormally high bile-pigment content, and at times were almost black. Urobilinogen and urobilin were always in excess—striking evidence of liver pathology. There was also in the duodenal contents a large amount of bile-stained cells, indicating an inflammatory process in the biliary system. The white count was never elevated; the red count diminished slightly; and the hemoglobin fell appreciably while under observation.

At discharge the patient was still losing weight and strength, was slightly jaundiced, and was in poor condition. The discharge diagnosis was infectious jaundice, with a question of early cirrhosis of the liver. The prognosis was undoubtedly very poor.

**Case III.**—John T. (E. M. 247,244), male, aged twenty-one.

*Past History.*—Gonorrhea six years previous, the discharge disappearing without treatment. Malaria two years previous to admission. Otherwise negative.

*Present Illness.*—This case should be considered together with that of his brother, Case IV, whose illness closely resembled that of the case to be described. Case III developed jaundice after an abrupt onset of gastro-intestinal symptoms. These consisted of anorexia, nausea, and vomiting, without abdominal pain. There was slight initial fever. The patient was admitted to the hospital two weeks after the onset of jaundice, with the above symptoms. There had been slight loss of weight, and pruritus was an annoying feature.

*Physical Examination.*—Physical examination revealed a well-developed, sick-appearing young man, deeply jaundiced, with linear excoriations on the skin. The liver edge was felt about 2 cm. below the costal margin and was tender. The spleen was not palpable.

*Laboratory Examination.*—The urine and stools were characteristic of obstruction to the flow of bile into the intestines. Several examinations of the urine failed to show spirochetes. Red count: 4,740,000 cells per cubic millimeter. White count: 4700 cells per cubic millimeter. Hemoglobin 111 per cent. (oxygen capacity). Differential count: Polynuclear neutrophils, 41.5 per cent.; polynuclear eosinophils, 3.5 per cent.; polynuclear basophils, 1 per cent.; large mononuclears, 11.5 per cent.; lymphocytes, 37.5 per cent. The stained smear showed no changes of importance in the red cells or platelets. Wassermann negative. Serum dilution: 1 : 120. Clotting time eleven minutes. Blood examination failed to reveal any spirochetes or malaria parasites.  $\alpha$ -Rays of the gall-bladder were negative.

*Course.*—The jaundice was intermittent in intensity during the month after entrance into the hospital, but never quite disappeared. There was no elevation of temperature in this period. The liver was observed to increase in size, however, and at the end of this time the spleen was just palpable. The patient's general condition gradually became poorer during the following two weeks, the jaundice deepened, and at the end of six weeks after admission slight tenderness was noted over the gall-bladder. At the same time there was a rise in temperature from normal to 102° F. During the next few days the temperature gradually dropped to 100° F., but the jaundice increased and the localized tenderness persisted. It was decided to perform a laparotomy, and operation was done about nine weeks after the onset of icterus. At operation the entire biliary tract was found to be involved in an infectious process, and the liver was grossly lobulated by fibrotic bands of tissue which traversed the organ in various directions. The gall-bladder and ducts were thickened. Cholecystectomy was performed, with drainage of the common bile-duct. Following the operation the patient's condition slowly improved, and the jaundice gradually disappeared. The red cell count, which had dropped from 4,700,000 per cubic millimeter on admission to 3,000,000 per cubic millimeter immediately preceding operation, returned to normal after a period of several months. At operation the hemoglobin

was 90 per cent. (oxygen capacity), a drop of 20 per cent. in less than two months, but did not return to a higher level coincident with the rise in the number of red corpuscles. Prior to operation there was a leukopenia; after laparotomy the white count gradually returned to normal, and the differential count, which had previously shown an absolute increase in lymphocytes and large mononuclears, also returned to its usual formula. The serum dilution dropped from 1 : 160 to normal (1 : 15) in two months.

A year and a half following operation the patient returned for further observation. There was said to have been no return of jaundice subsequent to the operation, and there had been a return of strength and weight. Physical examination revealed no jaundice. The liver was palpable 7 cm. below the costal border, was slightly irregular, firm, but not tender. The spleen was felt about 4 cm. below the ribs—evidently an increase in size during the period following discharge from the hospital. The red count was 5,100,000 cells per cubic millimeter, the white count was 6000 cells per cubic millimeter, and the hemoglobin 70 per cent. (Tallqvist). The serum dilution was normal (1 : 18). Examination of the stained smear showed no abnormalities in the formed elements of the blood except for achromia of the red cells.

One month following the previous examination the patient again returned. There were no abnormal symptoms except for loss of appetite and slight fatigue associated with undue exertion. There was a questionable icteric tint to the sclerae, but the liver and the spleen were the same as a month before. The red count was unchanged, but the white count was slightly lower—5200 cells per cubic millimeter. The differential count showed the following formula: Polynuclear neutrophils, 47 per cent.; poly-nuclear eosinophils, 2 per cent.; large mononuclears, 12 per cent.; lymphocytes, 39 per cent. There were many abnormal lymphocytes and mononuclears, and three of the latter were vacuolated. The platelets seemed normal. Serum dilution was slightly above normal (1 : 24), and the Gmeline test on the blood-serum was positive, giving definite evidence of an increase of bilirubin in

the serum. The van de Bergh test gave a faint direct reaction, also suggestive of some liver disturbance. Urine and stool examinations were negative. The fragility of the red cells in varying concentrations of salt solution showed hemolysis beginning at 0.38 per cent., and complete at 0.28 per cent.—an essentially normal reaction.

In view of the last reported findings, it is evident that there was a slight but definite jaundice, and apparently an abnormal constitutional reaction in progress, as evidenced by the change in the differential count. It is probable that there have been several slight attacks of jaundice since discharge from the hospital, although of such moderate degree as to pass unnoticed by the patient. The final outcome of the case is still in question, but it would seem logical to expect further complications from a progressive cirrhotic process in the liver.

**Case IV.**—James T. (W. M. 248,828), male, aged nineteen.

*Past History.*—Malaria one year previous, with no relapse. Otherwise negative.

*Present Illness.*—The patient was a brother of Case III, and became jaundiced within a week of the onset of his sickness. The initial symptoms were identical with those of his brother. Like him, he continued to become more jaundiced, and except for slight remissions he became progressively worse. In spite of the persistence and progression of his symptoms, he did not enter the hospital until two months after the first appearance of icterus.

*Physical Examination.*—The patient was well developed, but had lost some weight. His skin and sclerae were of a bright yellow hue from the intense jaundice. The liver was much enlarged and the spleen was palpable. Otherwise the physical examination was negative.

*Laboratory Findings.*—The urine and stools on admission were those of obstructive jaundice. Red count: 3,512,000 cells per cubic millimeter. White count: 2800 cells per cubic millimeter. Hemoglobin: 101 per cent. (oxygen capacity). Differential count: Polynuclear neutrophils, 70.5 per cent.; polynuclear

eosinophils, 1 per cent.; polynuclear basophils, 0.5 per cent.; large mononuclears, 9 per cent.; lymphocytes, 19 per cent. The stained smear showed some anisocytosis and poikilocytosis of the red cells. Serum dilution was 1 : 160. No malarial parasites were seen. Wassermann negative. Bleeding and clotting time normal.  $\alpha$ -Rays of the gastro-intestinal tract and gall-bladder were negative.

*Course.*—While under observation for two weeks there was little or no change in the condition of the patient. There was no elevation of temperature. Frequent duodenal lavage with magnesium sulphate solution, contrary to the usual experience in cases of infectious jaundice, did not produce a satisfactory drainage of bile into the intestine. On account of the favorable outcome in the brother's case, operation was advised, but was refused, and the patient was discharged from the hospital. Two months later, or some five and a half months following the onset of the disease, the patient returned and requested surgical interference. At the second admission the process had evidently progressed to a marked degree. The jaundice was still deep, the liver and spleen were larger than on the previous examination, and ascites was present. The red count was 3,200,000 cells per cubic millimeter, the white count, 2000 cells per cubic millimeter. Serum dilution was 1 : 250. Duodenal analysis showed only small traces of bile entering the intestine.

Operation was performed, and revealed a condition very similar to that found in the previous case. The gall-bladder and ducts were thickened. The liver was nodular and cirrhotic. Inasmuch as the patient was obviously a poor surgical risk, the gall-bladder was drained, but nothing further was done. Following the operation the patient ran an irregular temperature, and after a very stormy course died forty days later. There was a terminal septicemia. Postmortem examination revealed a large, firm, nodular liver of a mottled, yellowish-brown color. Microscopically there was necrosis of the liver cells, with some signs of regeneration, and considerable fibrosis. Examination of sections of the organ, after silver impregnation, failed to reveal any spirochetes. The spleen was large and fibrotic.

Analysis of the preceding cases indicates several points of interest. The history in each of the 4 cases is similar, and the diagnosis of infectious jaundice is warranted in each one. Two occurred in known epidemics and were different from the other cases in the epidemic in no way except as to the final outcome. The other 2 cases were clearly infectious in origin, occurring as they did within a week of each other in the same family. All 4 cases were characterized by a jaundice which persisted for many months, with exacerbations in intensity, but never with complete remissions. The 2 epidemic cases progressed to a point where the patients had lost weight and strength and where the ultimate prognosis seemed exceedingly bad. In the other 2 cases the progress of the disease led to a condition that was ultimately fatal to one, and nearly so to the other patient. Surgical interference in the latter apparently arrested the rapid course of the disease, although the duration of life is probably limited to a few years at the most. In all 4 cases the final result of the original infection was a serious liver disturbance in the nature of a diffuse hepatitis or a cirrhosis.

It has been the purpose of this communication to point out briefly the usual course seen in cases of infectious jaundice, and to stress the disturbing features in severe cases. In addition, an attempt has been made to emphasize the fact that serious complications, though rare, may occur in the course of ordinary infectious jaundice. Such complications are dependent upon extensive involvement of the liver parenchyma, are progressive, and usually have a fatal outcome.

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CLINIC OF DR. SAMUEL A. LEVINE

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**THE DIAGNOSIS OF PREPARALYTIC OR EARLY POLIO-  
MYELITIS**

THE proper diagnosis of infantile paralysis during the early stages of the disease before actual paralysis has set in is at all times most important. In any community where the disease is not very prevalent it will naturally be very difficult because the symptoms and signs during this stage of the illness are for the most part not like those met with in many acute infections. Since the large epidemic of infantile paralysis in 1916 the incidence of the disease has become sufficient to make it important for all physicians who do a general practice to keep the possibility of poliomyelitis constantly in mind, especially during the months of August, September, and October, when the disease is most prevalent. Sporadic cases occurring during the remainder of the year can be recognized by bearing in mind the points to be discussed below, just as well as those that develop during the seasons of the year when the largest number of cases do occur.

The great importance of the recognition of poliomyelitis during the first few days of the infection, before any paralysis at all has developed, becomes manifest when one appreciates that we have no satisfactory specific treatment once paralysis has set in. Considerable progress has been made in recent years of a reconstructive nature in restoring function to the previously helpless limbs by orthopedic surgeons, especially through the efforts of Dr. Robert M. Lovett, in connection with the work of the Harvard Infantile Paralysis Commission.

But a type of prophylaxis that is hard to gage or measure, which, nevertheless, I believe to be real and beneficial, consists of detecting the illness the moment infection starts, having the patient go to bed and thus sparing the body any unnecessary motion. It is not unlikely that in this way patients that otherwise would be up and about for a day or so and eventually become paralyzed, actually go through their illness without ever developing any paralyses or are not attacked so extensively.

As one of the diagnosticians on the Harvard Infantile Paralysis Commission, and while working for the Department of Health for the city of Boston, an unusual opportunity was offered during the epidemics of recent years for me to see a large number of cases of acute poliomyelitis in all stages of the disease; inevitably doubtful cases, definite early cases, and late cases were seen. It is the purpose of this short discussion to emphasize a few points that have been of distinct practical value in early diagnosis, and it is not intended to take up any elaborate or systematic survey of the complete symptomatology of the disease. There are a few positive findings that always should be looked for, which, if borne in mind, would enable the practitioner at least to suspect poliomyelitis.

When a definite flaccid paralysis has developed there is no difficulty in making a diagnosis, but it frequently happens that patients are sick for several days with very vague symptoms, often considered a mere cold or gripe, or some gastro-intestinal upset, and then suddenly present the paralysis which discloses the seriousness of the malady. During these early days the family is much concerned and the doctor baffled, and, as it so often happens, the attending physician is reproached for allowing the child to "develop paralysis" or for "treating the patient for the wrong disease." We shall see that it is not difficult to make a presumptive diagnosis of preparalytic poliomyelitis with a fair degree of accuracy in many of the cases and in this way hope to minimize the ravages of the disease.

As far as the symptoms during the early stages are concerned most of them might well occur in any acute illness, and therefore many of them are not sufficiently characterized to

be of diagnostic value. There are a few of these, however, that deserve special mention. It must never be forgotten that with acute poliomyelitis there generally is *fever*, and as a corollary to this, whenever there is fever that cannot be definitely explained otherwise, acute poliomyelitis must at least be given some thought as a possible diagnosis. Frequently, if the patient is seen soon after paralysis has developed, the temperature is normal, but if there is an appreciable preliminary or preparalytic stage of illness, fever is practically always present. The temperature need not be very high; it often is not more than 100° or 101° F. *Headaches* and *vomiting* are common complaints in this illness, but what is of distinctly greater importance is a story of *pains*. The child or adult (the disease is not at all infrequent now in grown-ups) will complain of pain, most frequently in the back of the neck, along the spine, down toward the lower back, in the limbs, or in the abdomen. The most characteristic site of the pain is the back of the neck, but, as one can see, it may be anywhere in the body. The pains are apt to be troublesome even when the limbs or body are at rest, but they are particularly exaggerated on motion and especially when the arms or legs are squeezed and moved or when the head is bent forward.

When we come to the examination of the patient, the findings are more important, more constant, and more helpful. Here we come upon signs that are not frequently present in other infectious diseases. It has been our experience that *stiffness of the neck* and resistance to flexion has been present in practically every case of preparalytic poliomyelitis. With this, the head frequently is held in a retractive position, but this is not always true. No matter what the position of the head, on trying to flex the chin on to the chest the patient will complain of pain, and the examiner will experience difficulty and feel the neck muscles stiffen up and limit motion. In addition, in most patients there is a *positive Kernig sign* as well. As a matter of experience the latter phenomenon has been less reliable, has seemed to be more doubtful of interpretation, and not as frequently present in proved cases of poliomyelitis as

the neck sign. Of course, stiffness of the neck and a positive Kernig sign are both present in any kind of meningitis, whether due to meningococcus, tuberculosis, syphilis, encephalitis, or epidemic parctitis. Occasionally these signs are also present in toxic meningismus, from any severe infections like pneumonia, typhoid fever, otitis media, etc., when occurring in children. Most of the diseases that produce meningeal symptoms, other than poliomyelitis, can be ruled out by other findings in one way or another.

One can see, therefore, that every patient with unexplained fever who has vague symptoms should be investigated for signs of meningeal irritation. If the case is one of poliomyelitis, despite the absence of any paralysis whatever, the probability is great that there will be found rigidity of the neck or the positive Kernig sign, or both. The reflexes during this stage of the disease may be of no assistance in diagnosis and more indefinite findings, like the aspect of the child, the pupillary reactions, etc., are altogether too vague to be of any help. All these considerations are particularly to be borne in mind during the months of the late summer and early fall when the disease is most prevalent.

If you find fever, with stiffness of the neck and positive Kernig, what should be the next step in diagnosis? It is impossible to rule out preparalytic poliomyelitis unless you have made a definite diagnosis of one of the diseases mentioned above by a general physical examination, such as mumps, middle-ear infection, pneumonia, etc. You must at this point do a lumbar puncture. This is absolutely indicated in any doubtful case presenting the above findings. There is ample evidence that the procedure is harmless except for the momentary discomfort to the patient and the slight headache that sometimes follows the puncture. It is indicated primarily because when properly done it establishes the diagnosis of poliomyelitis. If the examination of the fluid is normal one can be practically certain that the case is not one of infantile paralysis. I say practically certain because there are very rare circumstances in which the spinal puncture is done so early in the infection

that it is still normal on examination, then several days later the findings become positive. This is extremely rare. I have personally never had the opportunity of doing a lumbar puncture, finding it negative, and then having the patient subsequently develop poliomyelitis. In most instances the pressure of the spinal fluid is normal; the fluid drops out slowly through the lumbar puncture needle. In a fair number of instances, however, the pressure is greatly increased, and a tube of 20 c.c. or more of fluid is obtained in a few seconds. The fluid is always clear and watery when the procedure is properly done. When blood is obtained, it is due to trauma, and, unfortunately, this is apt to vitiate all subsequent examinations and render a positive diagnosis impossible. The cell count should be made of this fluid, for this is the most important finding in the diagnosis. If the case is not poliomyelitis, the count will be normal, that is, under 5 per cubic millimeter. If the case is positive, the cell count will be elevated anywhere from 10 to several hundred. Generally the figure will be from 30 to 100 or 200. There is no consistent relationship between the number of cells and the ultimate outcome of the case. The type of cells found will vary, depending upon the stage of the illness. It is not unusual to have a predominance of polymorphonuclear leukocytes very early in the infection. Sometimes the proportion will be about the same for the leukocytes and lymphocytes. Very quickly, however, after the original infection mononuclear cells predominate, and during the paralytic stage of the disease you may find only lymphocytes present. The last test of the spinal fluid is the globulin reaction. This is always positive if the disease is present, and it may, in fact, continue for a few weeks even after the patient is feeling pretty well and the cell count has returned essentially to normal.

From the above it follows that in a doubtful case a lumbar puncture should be done. If this is negative, infantile paralysis is ruled out. If the findings are positive and no other condition can be found to explain the symptoms, the patient should be treated for poliomyelitis. It has been said that no harm is done by lumbar puncture. This is true whether the findings are nega-

tive or positive. Naturally, following this course, one might pick up epidemic meningitis or other diseases, *e. g.*, occasionally mumps, encephalitis, syphilitic meningitis, and tubercular meningitis. These latter diseases can have spinal fluid findings identical with those enumerated above. Although the prime purpose of the puncture is to make a definite diagnosis, there is a therapeutic aspect of more importance. In the occasional case where the fluid is under a very great pressure, removing some fluid and thereby diminishing the pressure seems to me to have a beneficial influence on the disease. It is impossible to predict beforehand which case is going to have a high spinal fluid pressure. Having decided that we are dealing with preanalytic poliomyelitis, no matter how well the patient feels, absolute rest in bed is imperative. The ordinary hygienic measures that are customarily followed during any acute infection should be carried out. Mild sedatives should be given if the patient is restless. An ice-cap can be applied to the head for headache. A daily bowel movement is desirable, and for this a mild cathartic can be given. All motion on the part of the patient should be spared. It is my opinion that no specific medication has as yet been devised that has proved to be of value. Many of these patients go through the illness without ever developing any paralysis whatever. One should not think because of this that the diagnosis was incorrect. During every epidemic there probably are many more people who have the infection and never show paralysis than those who do. In concluding I want to discuss 3 cases of preanalytic poliomyelitis who were quite sick and who completely recovered, although at no time showing evidence of paralysis.

**Case I.**—C. S., a boy aged eleven years, had been in excellent health until two days before I saw him, when he complained of a little headache and stiffness in his neck. It would pain him on moving his head, especially forward. There was no vomiting or generalized pains. The doctor found a temperature of 101.2° F. on the following day and put him to bed and treated him symptomatically for a cold. I saw him forty-eight

hours after the onset, and found a well-developed boy complaining of slight headache. Otherwise he felt very well and was quite active and ready to be about. Temperature 100.6° F. General physical examination showed no paralysis of his limbs, muscles, back, or palate. Breathing was normal and there was no difficulty in swallowing. The deep reflexes and superficial abdominal reflexes were normal. Kernig sign was negative. The neck was slightly but definitely stiff. On the strength of the stiffness of the neck, the slight temperature, and headache a lumbar puncture was done. Twenty-five c.c. of clear watery fluid under markedly increased pressure were removed. Globulin reaction was positive. The cell count was 49, 55 per cent. of which were polymorphonuclear leukocytes and 45 per cent. lymphocytes. The headache, which was rather troublesome before the puncture, immediately disappeared. The next day the temperature was normal and the boy made a complete recovery, never showing any paralysis anywhere, and has been perfectly well for three years. (Numerous cases of paralysis were occurring at the same time in the vicinity.)

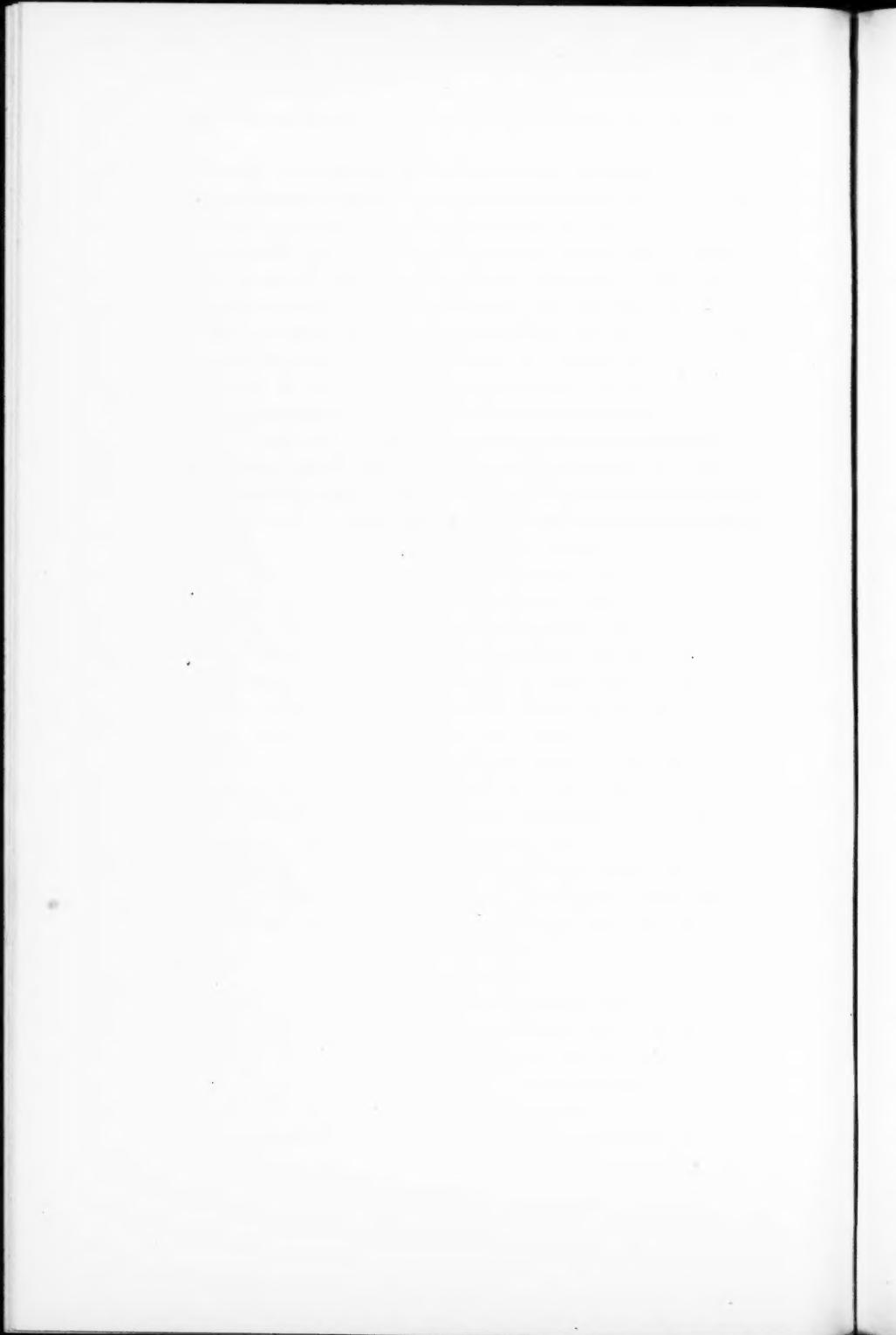
**Case II.**—M. G., aged six and a half years. This boy was living at a summer colony, and a few days previous to his illness 2 neighboring children died of poliomyelitis, and another came down badly paralyzed. Twelve hours before he was seen the child complained of headache and stomachache—he wanted to be left alone. Previous to this he was in excellent health. Temperature at this time was found to be 101° F. rectally. He vomited once, but complained of no pain in his limbs. General physical examination was negative. There was a slight apathetic appearance to the child. No pain on pressure or motion of the limbs. The Kernig sign was questionably positive. The neck was slightly but definitely stiff, but there was no pain on flexing the head. Lumbar puncture was done and 15 c.c. of clear watery fluid under moderately increased pressure were removed. Globulin + +. Cell count was 30, 80 per cent. of which were lymphocytes. The next morning the child felt perfectly well, temperature normal, and the headache had disappeared. He

was kept in bed for ten days and made a complete recovery, at no time showing any evidence of paralysis.

**Case III.**—G. G., aged seven and a half years. This girl was a sister of Case II. Five days after her brother took sick she complained of slight headache. The mother immediately took her temperature and found it 99.2° F. by mouth. She was put to bed directly and then felt quite well. She seemed to be bright and interested in things, although she complained of slight tightness in back of her neck. I saw her within twenty-four hours of the onset. Both knee-jerks were present only on reinforcement. The Achilles reflexes were absent on both sides. Throat showed no paralysis. Arm reflexes were present and the child could walk normally. Abdominal reflexes were sluggish. Temperature 101.4° F. by mouth. Respiration 48; pulse 124. Kernig sign definitely positive on both sides and the neck was definitely stiff. It was impossible to flex the chin on to the chest. Lumbar puncture was done and 8 c.c. of clear watery fluid were removed under normal pressure. Globulin was positive. Cell count was 12, 50 per cent. polymorphonuclear leukocytes and 50 per cent. lymphocytes. For the following two days the patient was very sick. Temperature 102° F. Respiration 60. The child seemed quite toxic, as if there was going to be respiratory embarrassment. Despite the marked hyperpnea, no evidence of weakness of the intercostal muscles or diaphragm could be made out. On the third day the temperature came down to normal, and from then on the patient made a complete recovery. During her convalescence the stiffness of the back was present and later slowly disappeared.

**Summary.**—It is possible to diagnose infantile paralysis during the early preparalytic stage with a fair degree of accuracy. This should be particularly true during the late summer and early fall when the disease is most prevalent, but the methods are equally applicable throughout the year. Every patient with unexplained fever should be examined carefully for stiff-

ness of the neck and the presence of the Kernig sign. If either one or both of these signs are present, a lumbar puncture must be done. This procedure is harmless, is indispensable in making a diagnosis during the preparalytic stage of this disease, and on occasions is beneficial to the patient when the spinal fluid pressure is increased. Performing a lumbar puncture will save unnecessary anxiety both on the part of the patient's family and of the physician. A normal spinal fluid practically rules out poliomyelitis. An increase in the cell count of the spinal fluid and a positive globulin together with other clinical features will enable the physician to make the correct diagnosis of poliomyelitis. In this way treatment and care of the patient will be instituted before paralysis has occurred and might help in actually preventing paralysis from developing.



## **CLINIC OF DR. HUGH GRANT ROWELL**

**FORMERLY DIRECTOR OF HEALTH AND HYGIENE, NEW BEDFORD  
SCHOOL DEPARTMENT, NEW BEDFORD, MASS.**

### **PROPER ADMINISTRATION AND CLINICAL MANAGEMENT OF SCHOOL MEDICAL WORK**

COME with me into the greatest of all clinics, the school, and there let us see and discuss a number of cases, some fairly common, perhaps, but exceedingly important in the proper management of school medical work, others observed from an unusual standpoint, and a few somewhat rare. We shall consider all from the point of view of the school as well as that of the clinician. Some types you may feel are not well worked up, but you must remember that these are later referred to other institutions or physicians. The pupils represent all social groups.

A PHYSICIAN: Before we begin to examine cases, will you discuss the methods of school inspection?

DR. ROWELL: Where organized, this is done by either part-time or full-time physicians with the assistance of school nurses and teachers.

A NURSE: What number of pupils can a nurse care for?

DR. ROWELL: The efficient nurse can handle 2000 children and do it well according to the Chambers of Commerce Survey.<sup>1</sup> If you give her more than that to care for you simply scatter her work over a larger field. As a matter of fact, they usually cover 3000 or more children. As to your nurse's responsibilities, that depends on her experience and training. We are too inclined to restrict her activities.

ANOTHER PHYSICIAN: What is the history of medical inspection?

DR. ROWELL: It originated in France in 1833 to provide sanitary conditions and to supervise the health of school children. In the United States the introduction in 1894 followed a series of epidemics among children of Boston. Then the primary purpose was elimination of contagious diseases. Since that time the fight has been turned against remediable physical defects, and recently the teaching of personal hygiene has become the third leg of the tripod of health. Sanitary inspection is one of the minor features.

DR. Z.: Will you tell us more of the methods in use?

DR. ROWELL: At first, most cities use the part-time system usually under the Board of Health. But, in spite of the conscientious efforts of many part-time inspectors, the vagaries of a few have been responsible for turning public opinion against this system. Usually there is too little check on actual accomplishment, and as a man's private work increases, naturally the side line suffers. Hence, if part-time men are used, the most desirable are the young physicians just out of medical school (or better still, the hospital) with their up-to-date methods or the retired practitioner whose interest will be in his enjoyment of the work. The conscientious worker will never receive adequate pay. Therefore the part-time man must consider it much the same as a hospital appointment where he makes definite sacrifice of time for the prestige and experience offered. The full-time man need not meet this problem because his time is spent entirely in the school system. Therefore he does not have the excuse of other calls for hurried or careless work.

The full-time department is now the ideal method and promises to continue so. Whether the city is large or not is immaterial. With a suitable system one man can handle a large population and other physicians can be added as needed. Detroit has developed a method somewhat resembling the group system of medical practice. Results are assured.

DR. M.: What is your general impression of school health work?

DR. ROWELL: We must remember that this field is largely untried. I have found the need and, therefore, I established

research in our department because we could not get the information by other methods. Most of the direction is done at present by educators with limited medical knowledge or medical men without knowledge of technical education and apparently little desire to acquire it. The problem now is to combine the two fields, and it is no easy matter.

Being a member of the school department I am able to get the teachers' angle on most schemes, and between their opinions and mine there is always a middle course which can be safely traveled. This co-operation is very necessary for successful field work. We need the other medical investigators, but, unfortunately, they have only in rare cases fitted themselves into a school system, become a part of it, and thus made their ideas practical.

**ANOTHER DOCTOR:** Do you have difficulty with the general practitioner?

**DR. ROWELL:** Recent articles<sup>2</sup> have criticized the medical profession for its lack of co-operation and even hostility in problems of public health. Personally, I do not agree with that view. This is comparatively new work, especially is the scientific basis new—and there are reasons why the general practitioner might view it with disfavor. Thoughtless deeds of the school physician or nurse are sometimes to blame. The speed expert who hustles over a large number of cases in the briefest period creates a doubt as to the quality of his opinion. (The teacher, too, will feel it is useless to refer cases to such a man, for he gives the pupil no real service—he is in and out of her room before she can even recollect what she intended to call to his attention. That school will be rapidly covered because the doctor will probably never hear of the work to be done.) Sometimes, also, the point of view of this work has not been made clear to the man in practice, and until he understands the matter he scents competition rather than correlation.

**MISS B.:** What about records?

**DR. ROWELL:** Notice each child presents me with a large white card usually folded double, about 8 by 5 inches. This contains the records of all previous findings in the school. Re-

garding the card, it travels from room to room and school to school with the child, and is eventually filed at my office (Figs. 118, 119). The teacher finds that this complete record explains

The Commonwealth of Massachusetts													
DEPARTMENT OF EDUCATION													
PHYSICAL RECORD													
Name	John Doe	Parent	Charles										
Address	46 Flint Ave.	Town (City)	New Bedford										
Date of Birth*	3/28/15	Sex											
Place of Birth	New Bedford	Birthplace, Father (Country)	U.S.A.										
		Birthplace, Mother (Country)	France										
Date	7/2 9/2	Throat, Tonsils and Other	—										
School	2nd	Nose, Adenoids and Other	✓										
Grade	I	Glands	—										
† Appearance	E	Heart	✓										
† Mucous Mem- brane, Color	E	Lungs	✓										
† Nutrition	P	Feet and Spine	✓										
† Posture	P	Nervous System	✓										
Scalp	✓	Mentality	12 90										
Skin	✓	Examiner (Initials)	RK										
‡ Teeth	C3	KEY — ✓ — Normal, — — Defect, + — Improved, ⊕ — Corrected, W — Notion.											
		* Write dates as follows: 3/28/23.											
		† E, O, F, P, (Excellent, Good, Fair, Poor).											
		‡ C — Carious, P — Filled, I — Irregular, M — Malocclusion.											
(CARD MAY BE FOLDED HERE)													
Grade	I												
Date	7/30												
Height	49"												
Weight	50lb												
Date	7/15												
Height	49"												
Weight	57lb												
Date													
Height													
Weight													
Date													
Height													
Weight													
Date	9/20												
	R. L.	R. L.	R. L.	R. L.	R. L.	R. L.	R. L.	R. L.	R. L.	R. L.	R. L.	R. L.	R. L.
Eye	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20
Ears	NN	NN	NN	NN	NN	NN	NN	NN	NN	NN	NN	NN	NN
Eyes; other abnormalities													

Fig. 118.—One type of record card.

some of her difficult teaching problems and the custom in some of my schools of marking the mentality with the I. Q. (intellectual quotient) or the relation between the mental age and the

chronologic age, has enabled her to classify her pupils more satisfactorily. This is of great advantage in a system where every

Record of Defects Requiring Treatment			Personal History		Names of Other Children in Family (first name)
Date	Defect	Treatment	Date		
9/30 '22	Dark brown spots on back of neck		Vaccination	9/12 '22	
	Dark purple spots on back		Chicken Pox		
	Shoulder blisters		Measles		
	Injected T.C. from	Card to parent	Mumps		
	sized glands at Z.	T+A	Whooping Cough	10/18	
			Scarlet Fever		
			Convulsions		
			Poliomyelitis		
			Tuberculosis		
			Rheumatism		
			Diphtheria		
			Schick Test	10/30 '22	Neg.
			Toxin Antitoxin		

Notes: 9/30 '22 Nutrition syndrome case.

HOME VISITS (MEMORANDA OF NURSE)			
Date	Reason for Visit	Information Secured at Visit	Result of Visit
10/6 '22	General physical condition	Secured cooperation	T+A

Fig. 119.—Reverse side of card.

endeavor is made to teach the child as an individual, giving it opportunity to advance as rapidly as its ability permits.

THE NURSE: Shall we begin the clinic with a common but important lesion?

**DR. ROWELL:** This girl of seven doesn't look very clean and appears a little ashamed of herself. You can see at a glance that it is simply pediculosis. Then why bring up such a case? Because in most schools, especially in a non-residential city, this is the commonest disease. We exclude the child, but the

Form HH 6

Saturate hair and scalp with kerosene and leave it on three hours. Wash off thoroughly with soap and water.

Remove nits with fine comb wet with vinegar.  
Do this every day for three days.

Molhar o cabello e casco com petroleo conservando-o assim por espaço de 3 horas. Depois lava-se bem com agua e sabão.

Limpar com um pente fino, molhado em vinagre, as lendeas, e isto por espaço de 3 dias.

Imbibez les cheveux et la peau de la tête avec du pétrole et laissez le pendant trois heures.

Ensuite lavez la tête avec de l'eau et du savon.  
Pour ôter les lentes servez vous d'un peigne fin saucé dans du vinaigre.

Répétez la même chose tous les jours pendant trois jours.

Zmoczyć włosy i skórę na czasie nafto i tak zostawić przez trzy godziny a potem wymyć całkowicie z mydło i czysto wodo.

Czesac włosy z gęstym grzebieniem namoczony w oczie aby usunąć gniidy.  
Trzeba czynie tak jak powyżej przepisano przez trzy dni.

Fig. 120.—A valuable home treatment for pediculosis.

problem is to get her back in school in the minimum time. I simply tell the nurse to give the child Form HH6 (Fig. 120). This avoids embarrassing the child by diagnosis and conveys an order to the nurse to make a home visit and demonstrate the approved treatment.

A VISITING PHYSICIAN: But why not send the case to a physician or a clinic?

DR. ROWELL: The children will not go, the parents believing the trouble of little consequence. In certain cases we would undoubtedly protect the family physician's rights.

THE NURSE: But why kerosene? Why not crude petroleum or tincture of larkspur?

DR. ROWELL: Kerosene is *supposed* to burn the scalp, but we do not find it actually does so. It is always in the household supplies. Either of the other drugs require purchasing, and this adds difficulties. The larkspur we do not advise because children are said to drink it, with disastrous results, and many homes are not very watchful. I doubt if we need to print in more than English, since many children frequently have to read the slips to the parents anyway.

The next child is eight, and he comes with his hands covered with clumsy bandages, extending over the knuckles. This picture alone gives us a hint that he is trying to conceal scabies. The irregularly placed red crusted dots over the back of the hands and forearms, less commonly papules and vesicles, plus the burrows between the fingers confirm our diagnosis, and the child tells us he has similar spots on his body. Our main interest is to get him excluded from school as rapidly as possible. His books are burned, with all his desk contents. That is the only protection which is sure. He is given Form HH28 which offers a choice of simple home-made sulphur ointment or a prescription to be filled at the drug store. The technic is that used in the Massachusetts General Hospital Out-patient Department with modifications (Fig. 121).

A PHYSICIAN: Why this particular prescription? What about balsam of Peru among the drugs?

DR. ROWELL: Question of expense. Most children use the home-made mixture anyway. This treatment clears up all except very bad cases in a week, sometimes earlier. Because of the danger of sulphur burns, in treating younger children, the

nurse has the family lower the percentage of sulphur. Frequently the ointment becomes the family panacea.

Here is a child with pediculosis combined with large crusted areas on the scalp, sometimes purulent. Both the occipital

Form HH 28.

**The Following Is a Good Treatment  
for the Itch.**

1. Remember the child can easily give the disease to the rest of the family.

2. Boil underwear, stockings, sheets and pillow cases, cloths and towels which the child has used, and iron the quilts and blankets twice with a hot iron.

3. For three nights rub the body very thoroughly with the ointment which you can get at a drug store with the prescription at the bottom of this paper OR else make a mixture of four parts Lard and one part Powdered Sulphur, thoroughly mixed, and rub this on the body but **not on the Head Face, or Neck.**

4. In the morning, after leaving the ointment on all night, take a warm bath with soap, and put on clean underwear, stockings, and other clothing touching the skin.

5. For two more nights repeat 2, 3, 4.

6. If the child is not cured by this time you should at once go to a doctor and keep the child under his care until cured.

.....

**To Be Filled at a Drug Store**

R

Sulphur	7.50
Beta Naphthol	7.50
Lard q. s.	90.
M	

Sig. Apply as directed.

Fig. 121.

and superior deep cervical nodes are enlarged, the former draining into the latter. I show it to illustrate a late stage which we find in neglected cases of pediculosis. It classifies as impetigo as much as the common facial type. Incidentally don't

confuse this deep cervical enlargement with a similar one from tonsillitis. A similar degree in scabies is shown in this other girl, on whose wrist near the base of the thumb you will notice several pustules. The ovoid scars near it represent the healed stage. Usually with the pediculosis, if we clear up the causative disease by the ordinary treatment, and then encourage frequent shampoos, the pustules will rapidly disappear, especially if we follow by ammoniated mercury ointment, half strength. They represent secondary infection from scratching. The same is true for the lesions in the scabies case just mentioned. Sometimes with scabies, however, this skin effect is simply the persistency of the disease with consequent vigorous treatment, and as in the cases of dermatitis medicamentosa, especially early ones, of which this may be said to be a type, the best treatment is to let it alone and see that the parent does so too. The parents frequently feel a case is neglected unless some drug or ointment is given, and will try some themselves if need be.

Regarding scabies and ringworm a most interesting article has just been published about their prevalence in monkeys and the communicability between monkeys and men.<sup>3</sup>

Another case, an end-stage, closes our series of infectious diseases. As you examine his body you will note that on the back, where it could be reached with the hands, and in front along the anterior axillary line are linear scars, now become white, while the whole skin in these regions is of a brownish dirty tinge. This is the old friend "vagabond's disease," and is said to be a result of the combination of dirt and pediculi. It is most common among tramps. The boy is now fairly clean and is going to work. In examining 1300 children of his age in six months this is the first I have found.

DR. X.: Do you see any rarer skin cases?

DR. ROWELL: Yes, here is one which fooled us all for a while. Only through the keenness of the nurse was the diagnosis finally made clear. Before I saw him the diagnosis of alopecia areata was made, and it is said that the appearance was typical.

He was given home treatments under the advice of a neighbor and the disease was not only arrested, but the hair began to grow back over the spots, and in September, 1922 he was shown to me by a nurse as a splendid example of alopecia areata. I, too, believed it to be the lesion. In February, 1923 I re-examined him, and found that there were several spots in the occipital region where the hair was again beginning to fall out. In other spots there were stumps of broken off hairs about  $\frac{1}{8}$  inch long. The skin surface of the bare areas was usually smooth, but in places irregularly scaly. On the lower edge of each area, occupying about one-eighth of its surface, was a definite inflammatory reaction. This is the typical picture of ringworm of the scalp in a fairly early stage. In April, 1923 it was still easily diagnosed. Evidently no one had previously seen the case with the inflammation, and without this the diagnosis of alopecia was a likely one. *x*-Ray is sometimes used, giving a definite epilating effect on the lesion, and is followed by local treatment, which must be exceedingly thorough. The present trouble was a recurrence. Unfortunately, no laboratory work could be done.

DR. Y.: That next boy looks perfectly well.

DR. ROWELL: This boy of fifteen, on examination, revealed both arms and upper arms, posterior surfaces, covered with slightly acuminate papules, extending on the upper arm as far as the deltoid insertion. Around the elbows and knees the skin was dry and harsh, suggesting ichthyosis. The abdomen, lower back, and buttocks, as well as the anterolateral and posterolateral surfaces of both thighs also showed the lesion, but on the legs it was more furfuraceous. The boy was worse in winter when this disease is said to be at its height. He claimed to note particular climatic difference. (Another case also said the lesion of his knees was worse in cold weather.) Diagnosis was characteristic keratosis pilaris superimposed on ichthyosis. The former lesion is a hyperkeratinization and is often associated with the latter disease. Its important differential diagnosis is from goose-flesh and syphilid. The boy was born with this skin condition and his mother also had it. An examination in spring showed definite decrease of the process.

Examine this boy as a neoplastic curiosity rather than anything else. His entire back is covered with a port-wine color homogeneous lesion extending from the buttock to both shoulders and up to the hairline of the neck. Throughout the colored area is distributed freely black soft hairs of about an inch in length. On the upper arms and on the buttocks and posterior portion of the thighs are similar areas varying in size from a quarter- to a half-dollar. This, of course, represents the port-wine colored mole and is well known to us as an occasional precursor of the melanotic sarcoma, although the growth commonly remains inactive. Stelwagon calls this type the "bathing-trunk" variety of nævus pilosus. At the present time no area seems proliferating and there is no present reason to believe that metastases are beginning. The condition has persisted since birth. As would be expected, no glandular enlargement can be found. In such a case the prognosis can rarely be changed by appropriate treatment, the lesions being too large and extensive for even the most daring surgeon to remove, nor could any plastic operation possibly cover the flayed area if this were done. The boy would hardly warrant great effort in sending him to the larger clinics because of the extensiveness of the lesions. Radium has been used successfully, but in a case of this extent the number and frequency of applications and the long period required for covering the entire area would militate against eventual success.

**AN OPHTHALMOLOGIST:** May I ask about your methods of eye conservation?

**DR. ROWELL:** Eyesight we must constantly guard, and our children are examined at least once a year, and notices of any defect sent to parents. A home visit is also made. The majority of cases are myopia, and are often suspected from unusual bending over their work. The test is simply the Snellen chart, although in younger children unfamiliar with the alphabet we use the same letter in different positions on the chart (E P A W), and the child demonstrates what it is by the fingers or by means of a single letter on a card which it holds in the hand.

Far-sight is harder to detect. We get the suggestion from afternoon headaches. To make a rough diagnosis we have them look in the distance and find they see distant objects more readily than those nearby.

Effort is made to have the light come from one source over the left shoulder or to use semi-indirect artificial light, never both. Most school-rooms are too wide, so that the inner third is not well lighted. That is a matter for architects to consider. Glass area should be one-sixth to one-fourth of the floor space. Windows should reach nearly to the ceiling, but be fairly high from the floor (about  $3\frac{1}{2}$  feet). Shades should be on a fixture which permits adjustment from the bottom as well as from the top and should be of a soft dull color. Shiny furniture is taboo.

One difficulty we find is that once having purchased glasses, a parent cannot see the need of changes in the lenses. Likewise, children do not like glasses and will avoid wearing them whenever possible, also, will delay repairs when they are broken. Frames have to be adjusted frequently in order to permit central vision, and I rarely go into a room where there is not a child or two who needs this service.

I see a number of leukomas, infantile cataracts, and traumatic cataracts. Strabismus is frequent and may be greatly helped with suitable glasses. If these fail, we can consider operation. We have one case of aniridia (or absence of iris), said to be one of two cases in the state. Blepharitis is common, less so pink-eye and conjunctivitis. A small epidemic of the former arose from carelessness regarding our principle of individual articles for individual pupils.

Where there is a marked progressive defect or where one eye is practically blind and the other only fair, we place the cases in *conservation classes*. Here they have large type in their books, special adjustable desks, and a room made physically ideal. They are taught to use hands in place of eyes whenever possible. Basket and other raffia work is done. We do not teach typewriting, for we feel such children would have difficulty in holding jobs, thus resulting in great disappointment. A few cases are able to leave the classes, but, in general,

these children have none too bright an outlook, and the poor boy with congenital aniridia is simply becoming blind by slow degrees. Braille is not taught because these children strain their eyes watching it, since they insist on trying to use eyes and finger-tips. Braille is for the blind only.

I saw a curious case the other day. A child absolutely well and whose eyes last fall tested normally, suddenly cried out and said he was very dizzy. The spell lasted but a moment. He had no aura, was not unconscious, and has had no attack in the two weeks since examination. On testing him with rough examination by getting him to hold the head steady and look to the sides and up and down, I found that when I had him look upward suddenly he had a combined nystagmus in both eyes, the motions being up and down and circular together. At the same time the exact sensations of the previous attack were simulated. He was referred to an eye specialist, and I believe will get considerable relief with proper glasses.

No school clinic is complete without a discussion of *nutrition* cases, and these we divide into the hygiene, pretubercular, and toxic groups. This pale, thin-faced boy of ten is a common type. (To the teacher.) How much is his weight this month?

THE TEACHER: He weighs 55 pounds. How much should you weigh, John?

JOHN: I should weigh 68 pounds.

DR. ROWELL: You will notice that both teacher and the boy himself know the proper weight. The interest of the teacher is essential. (To the nurse.) Have the other investigations been carried out?

THE NURSE: Yes. You remember you said the throat and teeth were normal and you saw no evidence of other pathology. The report from the TB. expert says the chest is normal.

DR. ROWELL: We work in close co-operation with the Board of Health TB. clinic, which, in addition to referring children to our Fresh-air Classes and passing on those suspected, will examine the chests of any nutrition cases in order that the Koch bacillus may be ruled out. (To the nurse.) What about your home visit?

**THE NURSE:** I found home conditions bad, but improving. The father had been out of work for several months, but has just secured a job. They have never believed in sleeping with open windows nor has the diet been a suitable one. The child has frequently been given a dime to buy breakfast and has purchased a bottle of "pop" and an ice-cream cone. There is not any regular bedtime for the child. I found them co-operative, however, and believe adjustments will be made. The work for the father will probably mean better food. I expect to visit them again in about a month.

**DR. ROWELL:** This method of investigation is used and definite disease ruled out as far as possible before the simple diagnosis is made. Regarding height, we use the Wood standing height for measurements because the scales, which are in every school, are so fitted and it is much simpler than the "pelidisi" or sitting-height-to-weight ratio of Pirquet. I agree with Dr. Baker that the combination of weighing and physical examination is the best.<sup>4</sup> I use the Wood tables and standards. My own investigations proved Emerson's 7 per cent. criterion sometimes more all-inclusive than the 10 per cent., and we shall later use this standard when facilities permit.

Regarding nutrition clinics, the idea was tried locally, but died out in a year or so. For schools they involve so much record keeping and follow-up work that, unless a large force is available, methods less elaborate have to be used. As a matter of fact, we do most of the work required in a slightly different manner, the formal clinic and detailed records being simplified, but the cases closely followed. The milk lunch in our primary schools, especially those where the immigrant type of pupil is present, has shown marked value, the underweight children usually gaining consistently during the school year and approaching normal. There is a distinct difference in the progress of these pupils when they enter the grammar grades, where the milk work is not done. However, don't overdo milk and spoil the child's next meal.

Observe now this boy of fifteen. His family were tubercular, and at eight he was markedly underweight, so much so that

it was feared he was infected. He then had influenza, following which he spent a year at the local sanatorium, and when non-



Fig. 122.—Note the semirelaxed position afforded by the steamer chairs.

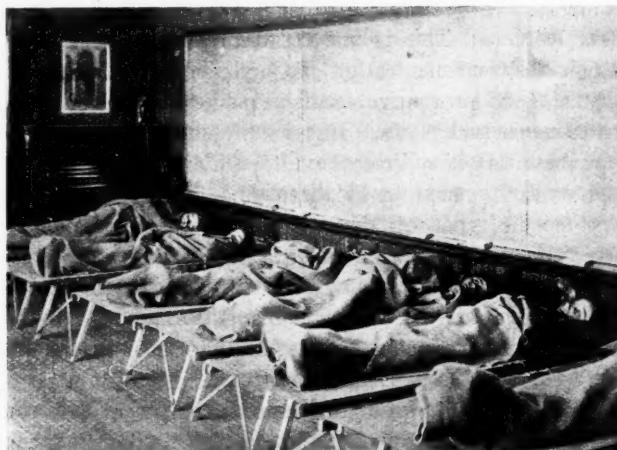


Fig. 123.—Absolute relaxation like this permits rest, even sleep. The cost is about one-third that of steamer chairs.

infectious was sent to our fresh-air class. These are open-window classes in portable buildings, conveniently located, because car-

fares are an important item in the success of this scheme. He had definite rest periods morning and afternoon sessions and was furnished milk. He and a number of other children, however, came to the afternoon session exhausted, and investigation showed that they were carrying dinners considerable distances to their parents. The session was then changed to a continuous one, and a warm lunch provided in addition to the milk. Since then gains have been more consistent. Regarding the rest periods, we have found the cot much more satisfactory than the reclining chair, and the children prefer them (Figs. 122, 123). Blankets are individual and carefully aired. They are laundered between terms. In these classes more ambitious records are kept. Weights are taken weekly and charted; temperatures as indicated. Each child is examined monthly by the Board of Health Expert.

**THE SECRETARY OF THE DEPARTMENT:** This boy looks as if he never had a sick day.

**THE BOY:** I feel that way, too. I am perfectly able to do anything.

**DR. ROWELL:** This is not an uncommon case where the situation has been met early. To my mind it shows the necessity of good preventive medicine and the schools are the place to reach such cases. Just at present I have a waiting list for these classes and may have to establish more. Cardiacs who live near them profit by the régime. Tubercular cases of the orthopedic type are admitted when vacancies permit and receive benefit. Children are discharged to the regular classes after the lesion is well arrested, but are known to the teachers and nurses, who keep close watch upon them, as does the TB. clinic. Universal weighing throughout the school system each month is enabling us to discover more cases.

To carry on successfully educators must work out some plan for open-air rooms in each school which will be available for those who need them. Because of grading, this presents certain difficulties. Also, most school systems are hard pressed for room. But, eventually, we hope this may be accomplished.

**DR. ROWELL:** Notice this boy of ten. In the fall he returned to school after a summer tonsillectomy, summer being the

open season for follow-up work. Last year he was constantly absent with colds, was pale, 18 per cent. underweight, and barely got his promotion. He had the operation early in the summer and practically lived on the playgrounds. (We have nine of these under our supervision.) Now he is up to normal weight, his color is good, the bean-sized glands at the angles of his jaws are reduced to pea size, and his work has greatly improved. The adenoid facies persists, but except for a little dryness of the throat and a rare and slight earache his is absolutely well.

THE NURSE: You might explain the last two symptoms.

DR. ROWELL: Dryness of the throat is not uncommon after tonsillectomy, the spongy moistener being gone, but it causes little if any discomfort except in a few neurotic persons. The earache is rare and does not persist. It is more common within a few days of the operation. Conceivably, this boy's diseased tonsils may have given him slight trouble with the ears as well, and the nidus being gone, the ear symptoms will disappear or greatly decrease. In the cases with deafness we could not guarantee improvement, but could usually promise arrest of progress.

The next child is six. The nurse has examined her throat and believes the tonsils are pathologic. As I look in the throat I notice a bit of tonsillar tissue, perhaps the size of a raisin, protruding from behind each anterior pillar. I find a pea-sized gland at each angle of the jaw. (To the nurse.) Why do you think she ought to have her tonsils out?

THE NURSE: The principal tells me she is frequently absent because of colds and sore throats.

DR. ROWELL: What other cause might exist for this? Perhaps you remember my mentioning it last Wednesday at our nurses' weekly conference when I discussed these cases.

THE NURSE: You mean deviated septum?

DR. ROWELL: Precisely that. Do you notice that the right side of the nose seems to function better than the left? Have the child bend his head backward and press the tip of the nose upward and backward and in a good light, you will notice a deviation of the septum to the right in the middle third.

THE PRINCIPAL: What do you recommend? An operation.

DR. ROWELL: Not yet. An operation now would injure the prospects for a good sized, well-functioning nose because of interference with the process of growth. She will simply have to get along as best she can by the use of local remedies till adult age is reached. Incidentally, I see a number of children with this lesion plus pathologic tonsils. If you urge operation, don't promise them too good results.

THE NURSE: Since you mentioned this type of cases I have referred less tonsil cases to you because I find the septum condition is common and is frequently the explanation of my doubtful children.

DR. ROWELL: This healthy looking boy of twelve, upon throat examination shows a moderately large pair of tonsils. He has one bean-sized gland at each angle of his jaws, but without further evidence I am in doubt what to advise partly because the adenopathy might be from pediculosis, only the latter usually shows enlarged occipital glands also. (To the boy.) Are you out of school much? Do you have many colds?

THE BOY: I'm not out very much, but I often have sore throats.

DR. ROWELL: Here is the indication for the operation because he is getting definite symptoms. We will notify the parents and the nurse will make a visit and talk it over with them.

A VISITING PHYSICIAN: How do you find the parents?

DR. ROWELL: Depends on the nurse and to a less extent on racial peculiarities. A good nurse is usually able to receive at least some co-operation. Our nurses have a distinct prestige with the families because in the last ten years they have proved their arguments by results.

In general, regarding tonsillectomy, I think we must admit that we get overenthusiastic personally. Unless I can prove to myself that there is very definite need for the operation, as shown by other signs than merely large tonsils, except in the obstructing type, I do not advise it. That is the only way you can get a high percentage of successes, and the man in public school work must be able to justify his opinions and procedures

at all times. Otherwise, he is the victim of severe criticism, and thereby may do school medical work great damage. When you see two large tonsils blocking the whole space from anterior pillar to anterior pillar, then do not hesitate to urge operation. Likewise, if there is definite disease shown by the tonsils and glands, or in the nutrition syndrome<sup>5</sup> case. But remember that a certain amount of tonsillar tissue is normal and, furthermore, even if it is a little larger than normal, if no symptoms exist, why crowd the clinic with these cases, and keep out those for whom the operation is a necessity? Deafness of any degree or even earache in the presence of enlarged tonsils or moderate-sized tonsils with a few glands always means recommendation for removal.

**x-Ray or radium** treatment has not yet proved an unqualified success, so for the present I should prefer to advise surgery. To me the pathetic case is the girl of ten with a double mitral lesion and enlarged but compensated heart whom I saw recently. The tonsils are definitely pathologic and we have tried for years to get permission for the operation. Now it is too late.

**A PHYSICAL INSTRUCTOR:** Are you going to omit our posture work?

**DR. ROWELL:** The question of posture in the school child is an exceedingly serious one and has been well studied by Goldthwait, Lovett, and Brown. Bancroft<sup>6</sup> believes we must begin about the second year of school to give definite posture exercises. As a standard of efficiency she proposes a "triple test" consisting of examination in standing position; then a marching test during which efforts are made to distract pupils' attention, thus causing them to resume their usual posture, and finally, the exercise test designed to show the strength and co-ordination of the muscles that are weak in posture, particularly those which hold the spine erect. For the last test an excellent exercise is a long sweep of the arms forward and upward, fully extended, returning them sidewise and downward to position at the sides. This method she believes much better than the "empiric" examination or general opinion of the cases. Miss P., what is our common posture defect?

Miss P.: The round shoulder, ptotic abdomen type, and one seems to meet it early in the school career and again in grammar and high schools. The latter is not due to lack of training, but rather represents one of the many problems of adolescence. Lee's work at Harvard showed this same condition in college students. The difficulty in public schools is that nutrition is frequently involved in our problem, and as we examine the pictures in Emerson's books we find that his undernourished cases present our common defect. The lack of nutrition results in definite muscle weakness as one would expect. This

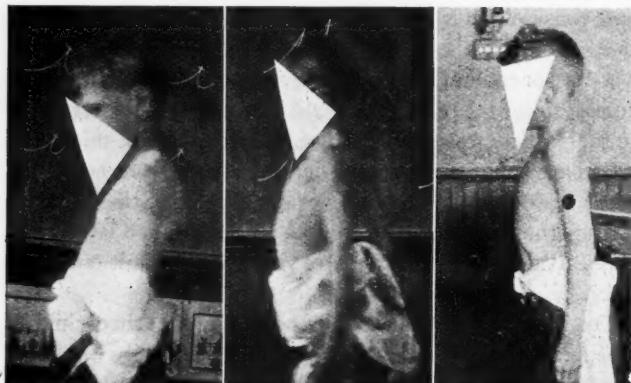


Fig. 124.—Two years of routine posture work. Shown at beginning and after one and two years. A real result.

being true, we must first investigate the physical welfare of the child before we classify it as only a posture problem. The physical instructor who fails to work with the school physician is sure to make grievous errors. On the other hand, some of us have the good fortune to find excellent co-operation, and here again the advantage of team work is shown.

Miss P.: These are pictures of a case which has given much encouragement to our workers and presents a fine example of the possibilities of team work between the health worker and the teacher (Fig. 124). This child entered school with fairly bad

posture, but not remarkably so. Health was none too good, and during the last of the year a rather brief illness, apparently the grippe, did far more damage than one would expect. On his return to school in the fall the posture defect was so marked that immediate plans were made for his future. Only the routine class exercises were used. The teacher agreed to keep constant watch and help the child to improve as rapidly as possible. Schrader, the State Supervisor of Physical Education in Massachusetts, and a man of large experience, has told me that he believes the routine exercises must always be done and any special corrective work should be given in extra time. Here no special exercises were used. In one year a marked improvement was made, the shoulder curve being much less and the abdomen less sagging. Improvement in nutrition came as a result of the exercises and improvement of posture. The middle photograph shows the difference in the child as the result of one year of care. Advance continued under the same system, and the last photograph at the end of two years more shows definite restoration to normal. Yet there are those who believe physical education is a "frill."

**DR. ROWELL:** Seating, correct class-room posture, and avoidance of weight-carrying of the type which will upset the balance of the spine also require attention.

In cases of extreme defects the examination by an orthopedic man is advisable and x-ray may frequently be needed to rule out tuberculosis. No such pathology being present, we can enroll the child in our posture class. We have at least one in every school to give the worst cases special work. One rather interesting boy presents a peculiar problem at present. He has about 9/50 vision in each eye, being a marked myope and astigmatic. His parents will not permit him to enter our eyesight conservation classes, so we have to do the best we can for him in the schoolroom. He is markedly round shouldered because of position required for seeing his books. All we can do is to conserve his vision as far as possible and give him special posture work. Exclusion from school would only make a greater difficulty for him and his parents.

Miss P.: In the posture classes we now keep track of cases through the use of the schematograph, a sort of camera which permits tracings of the spine to be made. These can be compared with later ones, and progress noted, more especially since we use a graph paper in making the record. But at present the system is confined to our posture classes only because of the time it takes.

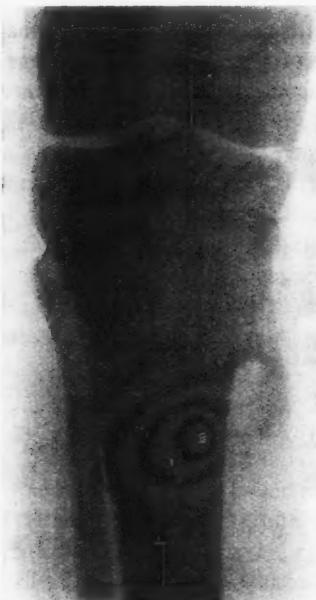


Fig. 125.—*x*-Ray of bone tumor. Anteroposterior view.

AN ATHLETIC COACH: Are there ever unusual cases in your football squad?

DR. ROWELL: Look at this *x*-ray of a boy I first examined early in September to determine his fitness to play football. He was perfect physically except for a small hard ovoid mass, the size of an ordinary marble, on the inner side of the right knee about 3 inches below the joint. He had always had this

and apparently it did not grow. It was slightly painful to touch. I advised *x*-ray and told him it was an osteoma, suggesting that he should at least have special padding over it. November 24th he returned to my office and said that whenever he kicked the football he felt pain in the region of the tumor. I again urged *x*-ray and advised him not to play any more until he was sure just what he had (Figs. 125, 126). A plate was taken



Fig. 126.—*x*-Ray of bone tumor. Lateral view.

by Dr. James A. Barrett, and the diagnosis of osteoma and osteochondroma was made. We advised him to cease football. Another physician felt that he would receive no harm, and he played through the season without injury, although he felt pain whenever he punted, and he was doing most of the kicking for the team. An operation was not advised at the time, but he decided to have one next summer.

Such a case represents a very definite problem to us, and, in my opinion, with this particular growth the boy should not have taken the risk of playing. On the other hand, I do not know of cases where such a growth has been broken off or where fracture of the leg has occurred under these conditions. The factor of turning an innocuous tumor into something more dangerous through constant blows necessarily received in bitterly contested games must not be forgotten. At any rate, all we can say is he apparently received no harm.

DR. Z.: Guess he was lucky.

DR. ROWELL: That reminds me of another football case of a much more serious nature. One of our backfield received a head injury in a scramble after the ball and was dazed for the moment. We at once withdrew him from the game. He insisted on sitting on the side-lines, but was not completely oriented and had marked diplopia. Pupils reacted normally and there were no reflex changes. After about fifteen minutes of rest he felt better, although still a little dizzy, with diplopia persisting. In another fifteen minutes he was still slightly dizzy and pulse continued slow. No apparatus was available for taking the blood-pressure. I was with him constantly to watch for signs of further disturbance, and was prepared to take him to a hospital immediately upon their appearance. No other neurologic changes appeared. We kept him out of the game in spite of his protests. He felt so well after the contest that he walked half a mile to the school, but there he suddenly began projectile vomiting. He was at once removed to his home and placed under the care of a surgeon. Neurologic symptoms were not remarkable. Plates taken the next day showed no sign of fracture. For about three days dizziness and slight but decreasing diplopia persisted, and then he was able to walk about. He returned to school in about a week, but it was several weeks before he was able to work normally. He played no more football during the season. This case represents an important injury not uncommon in football, and it is often difficult to determine whether we are dealing with a concussion, as in this case, or whether in another twelve hours we are going to be

thoroughly convinced that we have a serious fracture of the skull and surgical measures indicated, as in a similar case which I saw at the Massachusetts General Hospital. All these cases must be considered absolutely serious and, to my mind, are better in a hospital under a man who understands head work and where immediate care can be given in a surgical emergency.

DR. M.: Do you see many cardiacs?

DR. ROWELL: Frequently. Here is a boy who came to my office on his fourteenth birthday to secure a certificate that he was in sufficiently sound health and able to work as a cleaner in a textile mill. Incidentally we give them a thorough examination for these cards.<sup>7</sup> Cleaning is a fairly active job, requiring not too great output of strength. Five months previous the diagnosis of *organic mitral disease*, chorea, and rheumatism was made by a pediatrician. The hospital record tells only of a slight systolic roll heard over the apex. The day after the hospital examination tonsillectomy was done. Two months later, as a patient in a cardiac clinic, the diagnosis was rheumatic heart, Class B, inactive, with mitral regurgitation and chorea. Heart was enlarged to the left, the apex being 1 cm. outside the nipple line, sounds were of good quality, systolic murmur was heard at the apex and over the precordia. The child was thought to be able to attend school provided he rested for an hour at noon, and this he did.

On coming to my office he gave a past history of joint pains, twitchings, and dyspnea on climbing stairs, but said he could now run and climb three or four flights of stairs without losing his breath. The cardiologist who had previously seen him did not wish him to go to work as soon as this. Examination showed no enlargement of the heart, pulse at the apex was 92, often irregular, and a systolic murmur could be heard at the apex. Certificate was refused.

Two days later, in a conversation with the father, I discovered that the boy was constantly stealing and was in danger of court action. The father considered the situation hopeless. It was felt that some sort of work as a definite job might prove an effective remedy for this. The father agreed to return to the

cardiologist for opinion and also to have the hospital psychiatrist attempt to determine whether there was a mental defect behind the thefts. The boy did not impress one as absolutely normal, being somewhat fearful and shifty eyed, hence at that time of a rather unpleasing personality. I agreed that work would probably help, and advised the father to find some very easy task. In about a week he returned with the promise of a mill job which involved little activity and no physical strain. This day his pulse was 108, but more regular in quality. I passed him.

My impression was that here was a mild rheumatic heart case with excellent prognosis provided reasonable care was taken for a few months. Improvement had been marked since the tonsillectomy, and there was no reason to suspect permanent cardiac damage of any consequence.

About two months later I was going through the mill and met him again. He said he had absolutely no trouble at work and was feeling much better than when at my office. As a wage earner his morale also had improved.

Five months from the first examination he again appeared, this time for a card as wire-boy, which means great activity of the hands, but little for the rest of the body. Work is usually done standing. He now weighed 111 pounds instead of  $103\frac{1}{2}$ , his heart was normal in size, the rate was regular and was 72. He had been told at the hospital that he was in absolutely good shape. Character improvement was also marked.

This case is of importance in considering just how much leeway we can give these heart cases where the etiology is removed early. This boy had nine months, consisting of four of inactivity and five of the lightest sort of work, before he was allowed to perform tasks normal for his age. I believe such children with a careful régime early in their career can later take up many of the activities normal for their age. Nevertheless, I would hesitate to pass such a child for football or any strenuous sport without the strictest investigation, and probably not then.

John is seven and has *congenital heart disease*. He is constantly under a physician. The cheeks, tip of the nose, ears, and mucous membranes are cyanotic. He has definite club-fingers. His pulse is regular and 108. His chest shows pigeon breast. His heart is enlarged. No thrill is present. A rough systolic murmur is heard best to the left of the sternum, but also at the apex. Precise diagnosis is difficult. He has always been cyanotic, and on occasion becomes exceedingly blue, much to the terror of any teacher who has her first experience with him. For a while he was excluded, but experience has proved he is better in school, so he comes and goes as he chooses, rests when he desires, and suffers no physical harm. His peculiarities are passed on from teacher to teacher and his attacks of cyanosis no longer alarm anyone. Holt<sup>8</sup> seems to believe progress is good after six years of age. He would do better in a cardiac class, if we had one, but as it is he is well managed, in fact, a great pet.

Regarding cardiac classes the number of available cases must be fairly large since we need at least ten or fifteen to form such an organization, and the transportation problem is a serious one because the class ought to be within a very few moments' walk of the child's home or exceptional means of coming to the class provided. It should be said that a large percentage of cardiacs have physicians and are under their care.

A PEDIATRICIAN: What heart classification do you find satisfactory for school work?

DR. ROWELL: Halsey<sup>9</sup> has a workable grouping.

1. Organic cases able to carry on their habitual activity.
2. Organic cases able to carry on diminished physical activity:
  - (a) Slightly diminished.
  - (b) Greatly diminished. (These are doubtful cases for school.)
3. Organic cases unable to carry on any activity. With us, these cases would be excluded and probably would make no attempt to enter school anyway.

4. Suspected cases with abnormal physical signs or picture, but believed to have non-cardiac cause.
5. Potential cardiacs, such as choreics, syphilitics, cases of rheumatic fever, or tonsillitis.

I want you to regard this next boy, not because of the rareness of his disease, but because he represents the need of common sense as well as science in passing children for working certificates. He first came to my office when he was fourteen years, five months old. His color was a lemon yellow, he weighed 120 pounds, which was normal. Otherwise he seemed to be in good health. Heart examination showed no evidence of pathology, but sounds were very marked. The abdomen was moderately enlarged, however, no evidence of fluid could be found. A large mass in the left upper quadrant and flank, with definite notching extended 6 inches below the costal border. Liver was not palpable. As he lay upon the examining table he showed no dyspnea. He admitted he slept with two pillows. Diagnosis of *splenic anemia* or Banti's disease was made. He told me he had been at the Children's Hospital in Boston and that splenectomy was advised. The ideal time for this is, of course, before the liver is seriously injured. No guarantee of results was offered and the risk had been carefully explained to him. For this reason he decided to delay till he became markedly worse. At the time of his first examination he could play baseball and football and was still doing so. He wished to work as a helper in mercantile work. This is a very light task. The employer was a family friend and understood the boy's condition. For this reason he was passed.

AN INDUSTRIAL PHYSICIAN: What was the subsequent history?

DR. ROWELL: He reappeared two and a half months later with color greatly improved and weighing 122 pounds, or 2 pounds more than previously, although this was not necessarily a sign of better health. He was able to chop wood. The spleen was now  $6\frac{1}{2}$  inches below the costal border in the midclavicular line, but probably had grown little if any since previous exami-

nation. As before, no other abdominal organs were felt. He desired to work as a telegraph messenger boy, and he was passed for this, with the understanding that he was to inform his employer of the lesion (this was done) and that he would quit upon signs of trouble. Being co-operative and with sensible parents, this step offered no risk.

He remained at this work for a month, then quit chiefly because he did not care for it. He weighed 125 pounds, was of better color than on first appearance, but less good than the second examination. This time he wanted to work as a delivery boy for another family friend. He now became slightly dyspneic on lying flat on the table, but was relieved by two pillows. For the first time there was marked pulsation in the right suprasternal fossa, but none elsewhere. The spleen was the same size as at last examination. The liver, as usual, was not felt. Pulse was 96. Clinically, it was evident that the boy had lost ground, but not markedly. He was passed with the same understanding as before, but was told to report every month or two for further examination.

Laboratory facilities were not available, nevertheless the diagnosis is perfectly clear. Furthermore, our interest is in another point of view. The boy's desire for school work has ceased, nor is he capable of being a good student for both physical and mental reasons. He desires to perform some useful service while possible. He has been under excellent medical care both locally and in the Children's Hospital. His family know the situation and each employer is also familiar with it. He works limited hours. To refuse his certificate meant loss of morale to him and no good purpose was to be served. On the other hand, allowing him to perform light tasks permitted him to keep his mind off his disability and prevented mental invalidism. When the time comes that his disease gets the better of him, which at this age it may soon do, he will know enough to stop. This case shows some of the problems of the examiner, his relation to clinics and practising physicians, the desirability of his being furnished with excellent laboratory facilities, since the following of the blood here would have been of great value in

immediate prognosis. It also brings out the point that if we can control conditions we can be much more humane in our management of such children, and yet help rather than damage them by permitting carefully supervised tasks. And the best check on such cases is offered by the compulsory examinations required by the Massachusetts Labor Laws.

Consider this grammar school pupil as an interesting problem in anatomy (Fig. 127). Since birth the whole left arm and hand have been cyanotic, and rather mottled, not unlike the skin of a

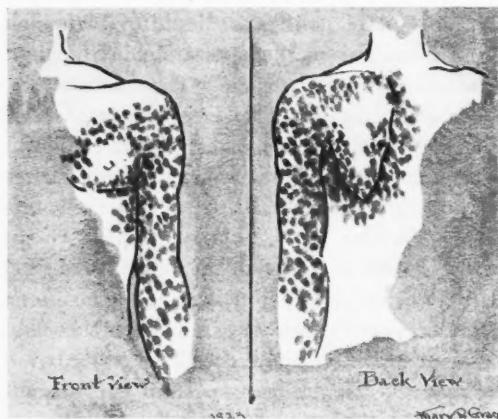


Fig. 127.—Mottled cyanosis of shoulder-girdle and arm.

limb after poliomyelitis, but more exaggerated in color. The bluish purple is also seen in the area about the left nipple, through the left axilla around the borders of the scapula. As shown, a few areas on the fingers are not colored. On two examinations this region was warmer than the paler areas. At another time it was the same temperature but more moist, and here it differs from the cold areas of poliomyelitis. Referring to our anatomy we find the whole supply of the region is from the subclavian artery, the internal mammary and its branches covering anteriorly, the brachial and its branches the arm; the transverse

cervical across the shoulder, and the surpascapular around the scapula. These branches all originate in the first part of the subclavian distal to the vertebral artery. The cause we can merely speculate upon, little history being obtainable—perhaps a difficult labor with injury to the vessels at the point named, less likely a nerve injury, still less probably a cervical rib if for no other reason than that the lesion is too extensive. It doesn't seem like a hemangioma. Trophic disturbance is an alibi, not a diagnosis. Unfortunately we cannot have an *x-ray* as part of our case.



Fig. 128.

Two cases represent small congenital deformities. The first has an enlarged plica semilunaris on both eyes, as you will notice by comparing it with the normal eye (Fig. 128). Such a defect represents the nictitating membrane or third eyelid seen in the eye of the cat and other lower animals.

This other child of fourteen has had two operations for tongue-tie and now speaks with little defect (Fig. 129). The end of the tongue has a sulcus through its entire depth, as shown in the diagram. The tongue arises from a paired anlage, near the

midline in the anterior part of the mouth. Our case, then, is one where the two halves failed to unite perfectly.

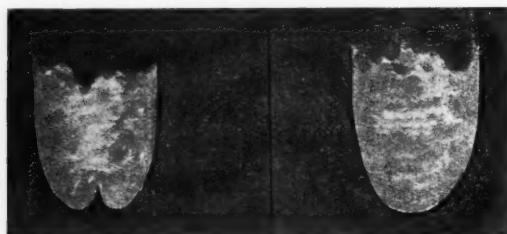


Fig. 129.—*a*, Tongue with bifid tip; *b*, Normal tongue.

Charles is in the first grade and is one of the brightest boys in his class. He has several congenital defects, as you will notice from the photographs. One hand is practically normal except there is a definite web between two of the fingers (Figs. 130, 131). The other hand has all the bones, but these are very



Fig. 130.—Dorsum of hands.

much smaller than normal and are easily felt through the skin. Yet with it he can grasp a pencil firmly and make some attempt at writing. To him it serves almost as well as a regular hand. Notice the full set of finger-nails. The foot, of course, is a uterine amputation. The family history is not remarkable.

This boy is a definite and interesting problem. He is bright and should be given every chance to make the most of himself by minimizing his handicap. The hand with the one web can be made an excellent one by a simple plastic operation. The other hand had better be left alone, since no improvement could be made (Figs. 132, 133). The foot can be greatly benefited by a suitable shoe. Now he tucks his stocking in the toe of his ordinary foot-wear and gets along with a limp. A special



Fig. 131.—Palmar aspect of hands.

shoe would not only improve his walking, but diminish the damage to his spine through the posture necessarily assumed in his present style of walking and standing. We shall try to do these things for him.

This is a fairly accurate drawing of a girl of twelve (Fig. 134). I did not feel justified in asking for a photograph, since she is just beginning to become sensitive about her condition and her troubles should not be increased. Fortunately for her she has



Fig. 132.—Lateral view of foot and leg.

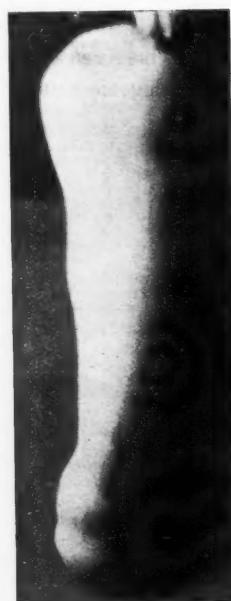


Fig. 133.—Anteroposterior view.



Fig. 134.—Head with double nose.

exceedingly good parents who will protect her in every way possible, and we are attempting to do the same thing in school.

There is the usual story of "marking," since this tradition seems to persist in spite of the disbelief of scientists. Originally she had a harelip and cleft palate. Operation was done for both and unusually good results obtained. Family history is negative.

Family history is said to show that the father and also several other members of the present generation have harelips. This I have been unable to verify personally.

The girl is markedly near-sighted, and this year was placed in one of our eyesight conservation classes.

Describing her face, we first note it tends to square outline, and this, combined with the wide distance between the eyes and the peculiar nose, gives it a bovine expression, more especially because the eyes are large, suggesting the classic "ox-eyed" person of Homer. The nose is broad and tends toward the flat. The septum appears to be double, and a definite sulcus in the skin between the two openings is unusually broad. The whole has the appearance of two noses from each of which one side has been removed, leaving the septum, and the two septa placed side by side to form an unusually wide partition and nose. Openings are patent and of ordinary size. Inspection of the inside of the nose shows nothing remarkable. There are no remains of the premaxilla nor are the teeth unusual. The plastic effect on the lip is good.

The whole picture suggests two heads, cut, one on one side of the midline and the other on the other, and the two larger halves united. All has been done for this girl that is possible. It remains to protect her from any influences which may make her sensitive of her condition. This will be a difficult matter.

A GRAMMAR SCHOOL PRINCIPAL: You might tell something of our troubles with the adolescent child.

DR. ROWELL: Two problems of the adolescent age must be definitely met by the school physician. The boy whose voice is changing must be protected against damage, and fortunate it is that singing teachers recognize this and usually leave the question of singing to the child's discretion. Our supervisor uses the clever system of never urging them to return to the

work after being excused for this cause, but giving a written lesson which requires considerable time and effort to prepare and present.

The adolescent girl is a more serious problem, especially since the diagnosis between certain hysteroid manifestations at this time must be carefully distinguished from epilepsy. Certain children have a very definite history passed along from teacher to teacher. A number of epileptic cases are clear cut and are definitely excluded, under home instruction if desired, and kept out until we are assured there will be no further manifestations. No single happening in a schoolroom is to be compared with the startling effect of a person launching into an epileptic attack. Teachers and pupils simply cannot stand it, nor do I blame them. These children move from school system to school system, but are rapidly discovered and excluded.

Several others, however, have presented different pictures. One case was permitted to return to school this fall after being excluded for attacks. Shortly after her return she suddenly became unconscious, without much other symptomatology, and to the principal she seemed almost pulseless. She was placed on a sofa, and on my arrival I found her rather pale, with a slow but steady pulse, no evidence, such as bitten tongue or history, to suggest epilepsy. The mother believed the attacks were brought on by arithmetic, this opinion being arrived at after her personal investigations. At any rate, no definite diagnosis could be made, but some hysteroid manifestations of adolescence were suspected and the parent was advised to keep the child at home the remainder of the school year, allowing her to study as she desired, but to have her live an exceedingly quiet life. She did well for several months, till a fire in her home started a recurrence of the seizures.

The last reports show attacks to be very infrequent and we hope by next year that she will be able to return to her work.

Another type at regular intervals disrupts the class-room by a characteristic seizure, apparently nothing more than fainting. One teacher solved the problem by the remark that the next time she did this he would "shove a bottle of strong ammonia

under her nose and let her stay in the class-room." Other less hard-hearted teachers had carried her to the rest-room where she spent the remainder of the session. At any rate, she now omits her attacks in the one class. No one until they have had a protracted experience with such a case can realize what a nuisance it is to the teacher and the health worker. Threatened exclusion until cessation of attacks sometimes works a marked cure. I suppose we must consider it an example of the unstable nervous and endocrine mechanism at this period of life. The element of malingering must not be forgotten.

A PSYCHIATRIST: How are the mental cases handled?

DR. ROWELL: The question of a child's mentality is rapidly becoming a matter which can be determined by the trained with reasonable ease. In one of our schools the determination of the I. Q. (intellectual quotient or the ratio between the chrono-logic and mental age) and its being recorded on the cumulative record card has proved of marked value to the teachers. Children three years or more behind their normal class are given special examinations first by our psychologist and later by the traveling mental clinic of the Massachusetts School for the Feeble-minded, after a thorough record has been taken, covering the family history, personal and developmental history, economic efficiency, social history and relations, and normal reactions. Both organic and mental defects are considered. On the basis of these examinations Fernald<sup>10</sup> divides the positives into six groups:

1. Continue in grade, in cases of more than twelve years of age without too obvious defects.
2. Needs special class where three or more years retarded, or over twelve and with marked defects.
3. Needs manual and industrial training, and this training must be of a type which fits the mentality, and may be the piling of bricks, use of a wheelbarrow, etc., for many. Facilities are often difficult to secure and many classes must depend on raffia, beads, etc., and hope for other work.
4. Needs social supervision and protection.
5. May become delinquent.

6. Needs medical attention. Instruction based on this classification will get the utmost for and out of the mental case.

THE PSYCHIATRIST: Do you find many of the common mental types?

DR. ROWELL: Once in a while we meet the commoner mental defectives, as one boy, who is always smiling cheerfully, is good natured, and does everything he is told, yet his whole personality and his every action reveals that he is simply an idiot. One hydrocephalic child is kept in school to get what he can. Another child spends his time crawling around his seat or constantly bending over under the desk, learns absolutely nothing, and in this, his first school year, we suspected at the beginning that he, too, was a mental defective of marked grade, but of more active type than the other case. Half a year in school showed he simply needed discipline. So you see we can be fooled easily. A fourth type I have seen was represented by a young child in the second grade who had been previously debarred from another school system. The attendance officer found she was not coming to school and that she had not been excluded locally. On arrival one morning she at once got into action, and by attacking the teacher and other children lasted less than fifteen minutes in the schoolroom. In the principal's office, while waiting for her parent, she constantly struck at anyone near her, scratching them if possible, and loudly screaming unintelligible remarks. On arrival I at once pronounced her dangerous, and the matter went through the usual official channels. These cases are quickly discovered, and so are not usually found beyond the first two grades.

School health work is primarily diagnosis as far as the medical side is concerned, and I think you'll agree the cases are varied. Usually and rightly someone else must do the treatment, since the competition with the practising physician or the clinic is neither fair nor desirable. We are merely a sorting system composed of physicians, nurses, and teachers which separates out the normals and attempts to get others to care for our ab-

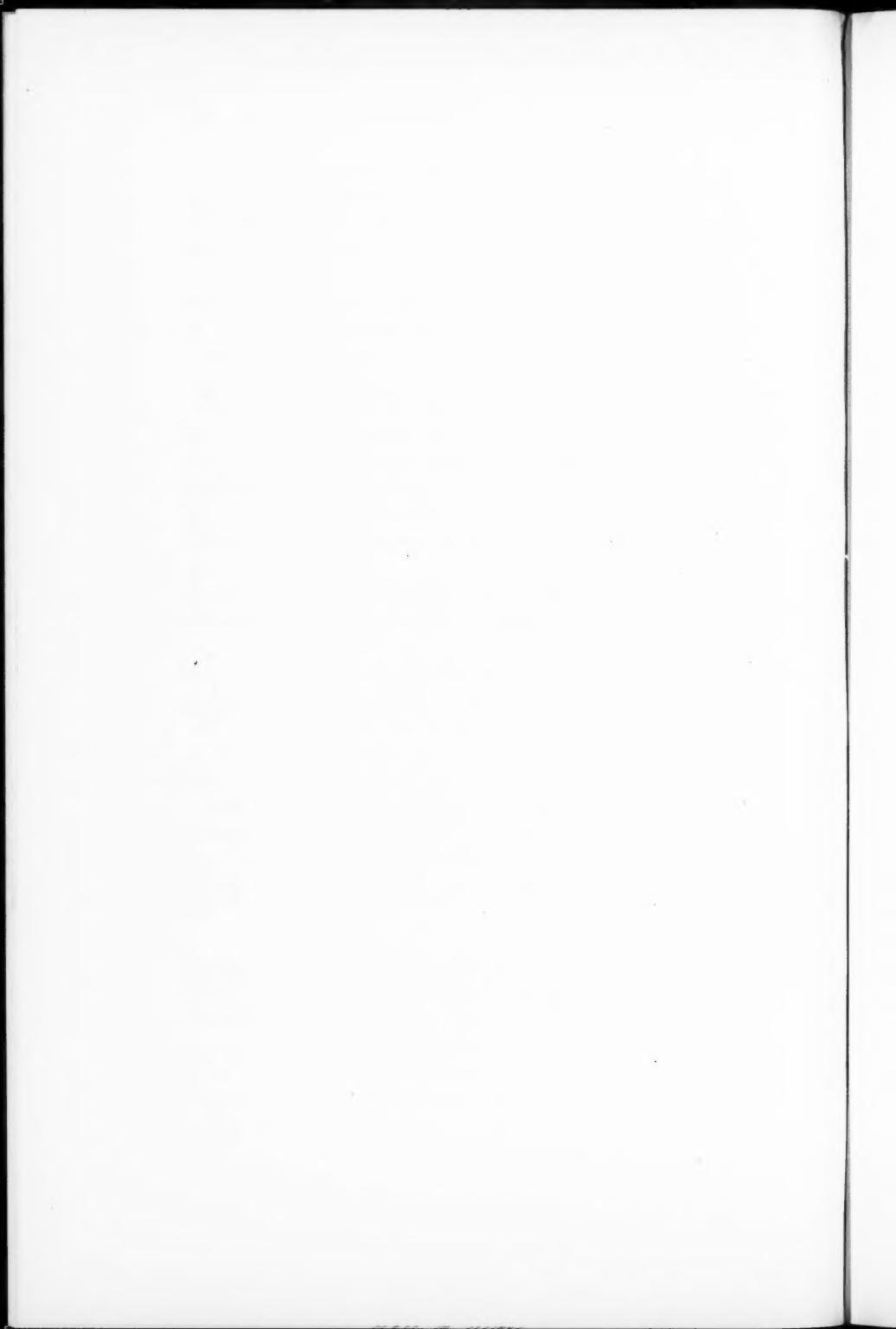
normals, except in first-aid cases of a minor nature or in the hygiene type of case which is essentially for the nurse to cover. Generally we do not have unusual facilities for diagnosis. The main thing is a finding accurate enough to get the child to some one who will study it further.

School health work is in its infancy. Some medical men consider it rather a farce. On the other hand, the variety of cases I have presented, the problems in diagnosis, the management of cases from the school point of view, and definite administrative duties show that the life of the professional school physician, whatever his title, is a busy one and one of the greatest value. His opportunity for improvement is unlimited, he has a clinic which is enviable, and exceedingly interesting problems for study at all times. I know of no field at present which offers a greater opportunity for the man who wants to be a pioneer and who has real training.

The ultimate success of this work will depend greatly on the interest and hearty co-operation of the rest of the medical profession.

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THE TWORT-D'HERELLE PHENOMENON (BACTERIOPHAGY); ITS POSSIBLE RELATION TO THERAPEUTICS\*

THE work of Pasteur demonstrated the existence of a whole realm of microscopic organisms which are parasites of man. Now, another Frenchman, d'Herelle, working at the Pasteur Institute in Paris, is attempting to prove the existence of another realm of *ultramicroscopic* organisms which are parasitic on the bacteria themselves. Or, figuratively speaking, to show that

"The big fleas have little fleas  
Upon their backs to bite 'em;  
And little fleas have lesser fleas,  
And so—ad infinitum."

Once given the possibility of parasites on bacteria, there immediately arises the hope of being able to use these parasites to kill pathogenic bacteria in the human body. What more beautiful therapeutic dream could there be than that of the treatment of streptococcal endocarditis, for example, by the intravenous injection of a culture of ultramicrobes whose sole function in life is the destruction of streptococci?

But this fascinating theory is far from being proved, and its practical applications are still, for the most part, dreams. We have only certain newly discovered phenomena in bacterial behavior which d'Herelle feels are best explained by assuming that the bacteria are being parasited by ultramicroscopic or-

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ganisms. D'Herelle's opponents, however, think that these phenomena are brought about by the bacteria producing autolysins and thus destroying themselves.

We shall, then, in this article take up:

- (1) The newly discovered bacterial phenomena.
- (2) Their relation to the clinical course of certain infectious diseases.
- (3) The two principal theories proposed to explain these phenomena, with the arguments on both sides.
- (4) The literature on the general problem.
- (5) The therapeutic tests which have been reported up to the present.
- (6) A discussion of the future therapeutic possibilities.
- (7) A statement of certain laboratory difficulties.
- (8) A summary.
- (9) Conclusions.

#### I. THE NEW BACTERIAL PHENOMENA

It seems best to consider first the main phenomenon; then two especially important accessory ones; and finally the other important and interesting observations, leaving out of this article a discussion of several disputed points.

The "Twort-d'Herelle phenomenon" is so named because F. W. Twort in 1915 was the first to report its discovery and because F. d'Herelle observed it independently of Twort, although he did not begin his long series of articles until 1917. The phenomenon is most easily demonstrated by d'Herelle's technic, which is as follows: Add to 50 c.c. of broth a bean-sized mass of stool from a typhoid or dysentery patient in early convalescence; incubate eighteen hours; filter through a porcelain filter; add a drop of this sterile filtrate to a cloudy broth culture of typhoid or dysentery bacilli, and incubate the contents of this tube for eighteen hours. At the end of this time the bacterial culture will have been completely dissolved, leaving a broth as clear as before it was inoculated. Now add a drop of this dissolved culture to another cloudy culture. In the same length of time, in this second tube, lysis

will have taken place exactly as in the first. A drop of this culture will then dissolve a third, and so on through hundreds of transfers.

The new phenomenon is, therefore, one of "transmissible bacterial lysis." *Lysis* of bacterial cultures is not new. But until Twort's work no substance had been discovered which would initiate "*serial lysis*." It should be noted here that each dissolved culture in the series can be filtered through porcelain before transferring a drop of it to the next tube, so that bacteria are not themselves being transferred from tube to tube unless they are ultramicroscopic, or "filter passing," as d'Herelle suggests.

One's first inclination when hearing of this new fact is to wonder at the remarkable potency of a substance which will act in "infinite dilution." Therefore it is important to realize that *no* substance *could* be so potent that starting with 0.001 c.c. in 10 c.c. of broth, and transferring 0.001 c.c. from this to another 10 c.c., and so on through 1500 tubes (as d'Herelle has done), it would be just as active, or even more so, in the fifteen hundredth tube. The "mathematical absurdity" of such an assumption is realized when one figures that if he desired to make in *one step* the dilution obtained in *only the twenty-second transfer*, he would have to place the 0.001 c.c. of substance in a "tube of liquid of such size that it would require a billion centuries for a ray of light to pass through from edge to edge" (d'Herelle). One must then admit from the first that new amounts of lytic substance are being formed in each tube. Transmissible bacterial lysis with active regeneration of the lytic substance is, therefore, the new bacterial phenomenon.

The first important accessory fact is that the lytic substance does not act uniformly throughout a culture, but concentrates its action at separate points. This is best demonstrated by spreading evenly over an agar surface a few drops of a cloudy broth culture soon after the drop of lytic filtrate has been added to it. After incubation the agar plate will show not a normal even growth or a total absence of growth, but a confluent growth through which are scattered few or many clean-cut, round, open

spaces, in which no bacilli are growing. These "holes" play an important part in d'Herelle's argument. To him each "hole" means a colony of ultramicrobes or "bacteriophages," and he thus claims to be able to count the "phages" just as bacteria are counted.

The second accessory fact is demonstrated by incubating the dissolved cultures for several days after they are apparently completely "lysed." Very often in such instances the broth will again become cloudy, giving the so-called "secondary culture." If this secondary culture is then plated on agar, two types of colonies will be found. The first type is round and consists of bacilli resembling the typhoid or dysentery bacilli which were used in the beginning. However, the organisms in this type of colony are more virulent, cannot be agglutinated by a specific serum, and are very "resistant" to the action of the lytic filtrates, but otherwise act like the organisms in an ordinary typhoid or dysentery culture. The second type of colony is "moth-eaten" in appearance, as if the edges of it were being "lysed." If these "deformed" or "moth-eaten" colonies are planted in broth, incubated, and filtered through porcelain, the filtrate will contain the active lytic substance and be able to initiate serial lysis. These colonies have, therefore, been called "lysogenic." Exposure to the action of the lytic substance, then, divides (or changes) a "pure culture" of typhoid bacilli, for example, into at least three different forms: a sensitive form, which is readily dissolved by the lytic filtrate; a "lysogenic" form, which either produces or "carries" the lytic principle; and a "resistant" form which, while still a typhoid bacillus, is far from being "typical." Besides these forms, by using lytic substances Gratia<sup>6</sup> has been able to obtain from a "pure culture" of colon bacilli eleven types of bacilli, differing in virulence, sero-agglutination, motility, mucoid growth, and fluorescence. This second accessory fact, namely, that certain individuals of a culture are much more sensitive to lysis than others, and that certain individuals themselves may produce the lysin, gave d'Herelle's opponents a different explanation of the "holes" from that suggested by d'Herelle. They have considered that

the hole represents a place either where "sensitive" organisms have been lysed or where lysogenic individuals have been active.

Many other observations have served to complicate the problem and furnish arguments for one side or the other. Some of these are given below.

**Sources of the Lytic Substance.**—Twort's original observation was on staphylococci obtained from glycerinated *calf-vaccine*. But since d'Herelle's work the main source of the lytic substance has been *stools*: stools of men suffering with dysentery of different types (Shiga, Hiss, Flexner, etc.), typhoid, para-typhoid A and B, and "infectious diarrhea" in infants; also from chickens with "chicken typhoid," buffalo with "barbone," and silkworms with "flacherie"; as well as stools of *normal* men and animals (horse, chicken, guinea-pig, rat, and silkworm). The substance has also been obtained from the *urine* of typhoid and pyelitis cases; from staphylococcus, colon, and anthrax *pus*; from *peritoneal exudate* produced experimentally in the guinea-pig by Shiga dysentery bacilli and *Bacillus coli*; from *blood-serum* of men with typhoid and dysentery, and normal guinea-pigs; from sterile *leukocytic exudate*; from *tissue extracts* of the small intestine and liver; from the *ferments*, *pancreatin* and *trypsin*; from *laboratory cultures* of colon bacillus and *Bacillus pyocyanus*, especially in *old cultures* of these and other organisms; from cultures of *two organisms* grown together; and, finally, from *earth, sewage, river-water, tap-water, and sea-water*.

D'Herelle claims that although there are many sources of the lytic substance, the intestine is in every case the *primary* source. If the lytic substance is obtained from urine, pus, serum, etc., it has been carried there from the intestine by means of the blood-stream; if it is in laboratory cultures, the cultures were originally obtained from animal bodies where they had become contaminated by "phages," giving what he calls a "mixed culture" of bacteria and ultramicrobes; while if it is in earth and water, it is because of fecal contamination.

**Properties of the Lytic Substance.**—The lytic substance has the same properties whether obtained from the original filtrates or from cultures which have been dissolved by these filtrates.

The activity of the lytic substance is practically unchanged by being kept sealed in the *ice-box* for three years, or evaporated to a syrupy consistency at *room temperature*. The substance will withstand *heat* to about 75° C., and can thus be separated from living bacteria, which are killed at 58° or 60° C.

Much has been written about the action of *chemicals* upon the lytic substance. Both d'Herelle and his opponents take arguments from this source, the one claiming that the "bacteriolytic" acts as a culture of living organisms, and the others that its reactions are those of a ferment. At the present time it would seem as if the substance were sensitive to quinin; could be extracted with 50 per cent. glycerin, though sensitive (at first) to pure glycerin; and is probably precipitated by alcohol. Many other experiments have been reported, but none of them are crucial.

The lytic substance will not pass through an ordinary colloidion *membrane*, but is said to pass through one made of 4 per cent. collodion.

**Non-specificity of Action.**—A given lytic solution is *not specific* in its action. If obtained from a typhoid case, its action is not limited to typhoid bacilli, but it may be equally active on one or more of the other members of the typhoid-colon-dysentery group. Its action will, however, usually be limited to organisms in that group. In a similar manner substances obtained from staphylococcus pus will usually, in the beginning, be active only for staphylococci. Lytic filtrates from *normal* stools vary markedly in their activity. One case has been reported in which a filtrate from a normal human stool would act only on the "bacillus of hog cholera." But no matter what organisms are originally affected, repeated transfers with other members of that group, or even members of other groups, will often make the substance active for these new organisms. Thus, a staphylococcus "phage" can be made active for colon bacilli, and vice versa. In such cases, however, the bacteriolytic will retain its activity for the organisms originally affected.

Up to the present time, by using various methods, lytic substances have been obtained for the following organisms:

Bacillus typhosus and B. paratyphosus A and B; B. coli; B. dysenteriae (Shiga, Flexner, and Hiss strains); B. proteus; Staphylococcus aureus, albus, and citreus; Streptococcus viridans and hemolyticus; Bacillus diphtheriae; B. pestis; B. pyocyaneus; B. anthracis; Pneumococcus, Types I, II, and III; Meningococcus; Micrococcus tetragenus; Bacillus subtilis; B. gallinarum (chicken typhoid); B. typhi murium; the "bacillus of hog cholera"; the pasteurella of barbone (in buffalo); and the coccobacillus of flacherie (in silkworms).

**Degrees of Activity.**—All filtrates active for a given organism, for example, the typhoid bacillus, will not have the same degree of activity for that organism. In some cases one may obtain a substance so active that 0.000,001 c.c. will completely dissolve a typhoid culture in a few hours. In other cases 2 c.c. will give no evidence of lysis of a broth culture, and the presence of the lytic substance is shown only by the demonstration of one or more characteristic "holes" when a few drops of the culture to which the filtrate has been added are spread over an agar surface and incubated. Between these two extremes there is every degree of activity. In fact, no two solutions are sufficiently alike to affect the same organisms to the same degree. But just as a substance can be made to acquire "virulence" for new organisms, so can its "virulence" for a given organism be, as a rule, increased. The same method is used in both cases, that of repeated transfer with the organism chosen, with filtration between transfers. Once a certain degree of activity is demonstrated, the solution will generally retain that degree of activity for that organism, no matter how long it is kept, or upon what other organisms it is made to act.

**Conditions Necessary for Lysis.**—To get the lytic substance to act upon the bacteria for which it is "virulent" certain conditions must be fulfilled.

First, *young, living* organisms must be used, preferably a three-hour broth culture. Dead cultures are not dissolved, and in old cultures only such bacteria as are living will be acted upon. Lysis will, however, take place if the young, living culture is suspended in normal saline solution.

Second, *complete lysis* will not take place if there are more than 500,000,000 organisms per cubic centimeter.

Third, the media must be *alkaline* to litmus, preferably having a pH of 8 to 8.2. A sugar broth which is fermented by the organism employed can, therefore, not be used, since in such a case the media will become acid.

**Relative Amounts of Substance and "Substrat."**—If, to a series of broth cultures containing the same number of bacteria per cubic centimeter, one adds increasing amounts of the lytic substance, the number of "holes" counted when a portion of the mixture is spread on agar and incubated will vary in direct proportion to the amount of substance added. But this is probably true only up to certain optimum concentration of "bacteriolysant."

If, on the other hand, one uses the same amount of lytic substance while increasing the number of bacteria with which it is put in contact, no change takes place in the number of holes until again one reaches an optimum. After this the greater the number of bacteria used, the less will be the amount of lysis which takes place.

**Observations During the Lytic Process.**—With a very active substance complete lysis of a bacterial culture will take place in from *five to eighteen hours*. During this time there may be alternate clearing and clouding of the culture, representing to d'Herelle's mind different phases of the struggle between the bacterium and its parasite.

If, from time to time during active lysis, preparations are made for *microscopic* study, the bacteria will at first stain normally with Giemsa stain, and then poorly. After this amorphous débris is present, together with granulations, spheric forms of bacteria, and occasionally long forms. Finally, there are no substances which stain.

If, immediately after adding the lytic filtrate to a culture of bacteria, this mixture is *centrifuged*, and a drop of the bacteria-free supernatant fluid is added to another broth culture, and a few drops of this culture are spread on agar and incubated, a certain number of "holes" can be counted. This shows that

"phages" are at first present in the supernatant fluid and have not been carried down with the bacteria. But if, after adding the lytic substance to a culture, one waits about three-quarters of an hour before centrifuging, the supernatant fluid contains no lytic substance and no holes can be demonstrated when a test is made. Lastly, if the culture is centrifuged an hour and a half after the addition of the lytic substance, the supernatant fluid when added to another culture will give about eighteen times as many holes as there were in the beginning. This experiment is interpreted by d'Herelle as indicating that the parasite was outside the bacilli at the start, penetrated the interior of some of the bacilli in about three-quarters of an hour, and there developed a colony of eighteen new parasites, which were liberated after an hour and a half.

D'Herelle adds another proof of this theory by observation with the *ultramicroscope*. At the end of three-quarters of an hour he reports the development in certain bacteria of about eighteen granules. The organisms containing these granules become swollen and spheric, and in about one and a half hours burst, liberating the granules. No other worker has reported ultramicroscopic observation, and we have no check on this experiment.

D'Herelle makes a final "counting experiment" in which he demonstrates the "*ultimate unit*" of the active substance, or, in his opinion, a single parasite. He dilutes the active substance to such an extent that a drop added to a certain amount of a bacterial culture will give only one hole on an agar plate. He then adds such a drop to 10 c.c. of a broth culture of the organism to be lysed, and divides the 10 c.c. equally among ten tubes. One tube will show lysis, while the other nine show no action by a lytic substance.

**The Antilytic Serum.**—It was, of course, natural that in these days of serologic study different observers should inject the lytic substance into laboratory animals in order to find out what "antibodies" would appear in the blood. The authorities realized that the results might be confusing because they had to inject not only the lytic substance (in which they

were especially interested) but also the lysed bacterial protein and the bacterial toxins and ferments. This being the case, antilysins, antitoxins, and antiferments might be expected to appear in rather confusing array.

Two facts about this "antiseraum" have emerged from somewhat contradictory reports. First, the blood from an animal injected with a lysed bacterial culture has a definite antilytic principle which, in test-tubes, either inhibits or completely destroys the activity of the lytic substance. Second, the "antiseraum" contains an *amboceptor* which will fix complement with an antigen composed of the lysed bacterial solution used in the injection of the animal. Whether or not this amboceptor will fix complement when *any* lysed bacterial culture is used as antigen remains a disputed point. There seems to be agreement that fixation will occur if the antigen comes from a member of the same group of organisms, but there is dispute as to whether the blood obtained from animals injected with a lysed solution of colon bacilli, for example, will fix complement when a lysed solution of staphylococci is used as antigen.

## II. CLINICAL OBSERVATIONS

It is interesting to note at what stage in the course of an infectious disease the lytic substances appear in the stools. *Early* in typhoid fever a substance is usually present which is quite active for colon bacilli, and perhaps dysentery bacilli, but is usually not active for the typhoid bacilli themselves. As soon as *convalescence* begins a substance appears which is active for the etiologic organism. Sometimes it will be active for stock typhoid cultures and not active for various strains obtained from the particular patient. In *fatal* cases d'Herelle claims that at no time does a substance appear which is active for the etiologic organism obtained from the case. This he explains by assuming either a very weak "phage" or a very "resistant" organism, or a condition of balance in which both a strong "phage" and a "resistant" organism exist side by side. This latter condition is found in typhoid carriers.

D'Herelle claims that at any time in the course of a disease

the patient's condition can be told by examining the stools, and determining whether or not there is present a substance active for the etiologic organism of the particular case. In his words, "In all cases the condition of the patient faithfully registers the vicissitudes of the struggle taking place between the bacteriophage and the invading bacterium."

If the lytic substance is injected *subcutaneously* in a normal person, it will appear in the stools in about twenty-four hours. The substance obtained from the stools will be in every way similar to the substance which is injected, and will be active for the same organisms. If these organisms are not present in the intestine of the individual injected, the lytic substance will be rapidly eliminated.

In studying epidemics occurring among animals d'Herelle demonstrated that the lytic substance could be passed from one animal to another, so that he believes there is such a thing as "contagious immunity." (This observation led him to believe that in epidemics among men immunity might be secured by putting enough "phages" into the water-supply to inoculate everyone.)

### III. THE TWO THEORIES

After two years of work d'Herelle formulated the following theory:

"The bacteriophage, *Bacteriophagum intestinalis* d'Herelle, 1918, an ultramicrobial parasite of bacteria, normally exists in the intestinal tracts of animals, both vertebrates and invertebrates. . . . An obligatory parasite, the bacteriophage, lives only at the expense of living, normal bacteria, which constitute its sole culture-medium. Experiments and ultramicroscopic examination agree in showing that the ultramicrobial bacteriophage penetrates into the interior of the bacterium, there forms a colony of fifteen to twenty-five elements within one and one-half hours; whereupon the bacterium bursts and liberates the young ultramicrobes.

"There is but a single species of bacteriophage, common to all animals, capable of acquiring virulence for different bacterial species, probably for all species.

"The existence of the bacteriophage in the intestine of all living beings, its exiguity, which allows it to filter through soils impermeable to bacteria, its vitality and resistance to agents of destruction, explain its extreme diffusion in nature."

Bordet, the most illustrious of d'Herelle's opponents and an upholder of the autolytic ferment theory, makes the following statement:

"Under some disturbing influence . . . a nutritive vitiation of the bacterium is primarily induced, testified by the appearance of the lytic agent. After this the interference of the external influence is no longer necessary. Henceforth the reproduction of the principle requires nothing more than the presence of living microbes which having absorbed a sufficient quantity of it liberate new amounts of the same agent at a certain stage of their evolution." . . . "Among the microbes thus touched a certain number are not immediately destroyed, and even—being still capable of multiplying before undergoing the lytic process—reproduce the lytic substance."

In outline d'Herelle's arguments may be summarized as follows:

1. *Serial lysis* can be brought about only by living organisms present in the original filtrates, and reproducing themselves in each new tube in the series.

2. The lytic substance is "*corpuscular* in nature," and its units can be counted. These units must, therefore, be living organisms.

Increasing the amount of substance increases the number of "holes."

Increasing the number of bacteria does not increase the number of "holes."

3. The lytic substance *does have* the attributes of a *living being*.

- (1) Its "virulence" is variable.
- (2) It has the ability to increase its "virulence" and acquire "virulence" for new bacteria.
- (3) It will adapt itself to conditions at first unfavorable, for example, the presence of pure glycerin.

- (4) Bacteria defend themselves against its action.
  - (5) Although it resists agents of destruction, certain living viruses are equally resistant.
4. The lytic substance does *not* have the attributes of a ferment.
- (1) It is non-specific in its action—ferments are specific.
  - (2) It is the same antigen, no matter what its source.
  - (3) It acts in proportion to its "virulence," not in proportion to its quantity as a ferment does.
  - (4) It can be obtained from soil and water, while ferments cannot.
  - (5) Its reactions to chemicals are different from those of ferments:
    - (a) It is sensitive to quinin—ferments are not.
    - (b) It is sensitive to glycerin—ferments are best preserved by it.
    - (c) It is destroyed by alcohol—ferments are precipitated by it.
    - (d) Its pH range is different from that of ferments.
5. Treating a lytic solution with *alcohol* precipitates a ferment which will lyse bacteria, but will not initiate *serial lysis*. Alcohol thus kills the "phage" and liberates its lytic ferment.
6. It is phagocytized by leukocytes, and is, therefore, foreign to the body and could not have been produced by the body cells, especially the leukocytes.
7. Its presence in other parts of the body than the intestine is explained by its being carried there from the intestine by the blood. Its presence in laboratory cultures is explained by these cultures being "mixed cultures" of bacterium and "bacteriophage."
- Most of the work of *d'Herelle's opponents* has given answers to his arguments rather than a clear-cut formulation of the arguments for their own theory. However, the following points are made:
1. The conditions which favor the development of the lytic substance are the same conditions which favor the growth of

bacteria; it is, therefore, natural to assume that the substance is a product of the metabolism of the bacteria themselves.

2. The substance in many ways resembles a ferment rather than a living organism.

- (1) It resists heat to 75° C.
- (2) It remains unchanged if kept in the ice-box and at room temperatures for long periods, even if deprived of bacteria, which d'Herelle says are its only food.
- (3) There is an optimum relation between the amount of the lytic substance and the "substrat" (the bacterial culture).
- (4) It is precipitated by alcohol.

The answers given to d'Herelle's arguments, taking up those arguments in the order given in the outline above, may be summed up as follows:

1. *Serial lysis.*

- (1) A similar phenomenon which does not require living organisms is that of *serial coagulation*. If uncoagulated plasma is placed in an oiled vessel it remains fluid. But when serum is added it will coagulate, and in so doing liberate a fresh amount of the coagulating principle, thrombin. This principle added to a new vessel of fluid plasma will coagulate it, and so on indefinitely.
- (2) Even if the regeneration of a lytic ferment does require living organisms in each tube, the bacteria themselves are present, and in this case produce autolysins. There is no need to assume the existence of another organism.

2. The "*corpuscular nature.*"

- (1) Even granting the corpuscular nature does not prove that the corpuscles are living beings, inanimate substances can be reduced to ultimate units. Perhaps in this case the corpuscles are "colloidal aggregates" in which the dissolved bacterial protein may play a part.

- (2) The demonstration of the "holes" is not proof of the corpuscular nature, since these may be explained by lysis of sensitive bacteria, or the activity of certain lysogenic individuals. (This argument, however, does not answer d'Herelle's point that in such a case the more bacteria used the more "holes" there would be. Nor does it prove that because certain colonies have been shown to "carry" the lytic principle, they are themselves the source of it, and hence "lysogenic.")
3. The *variability* of the ferment, its increased virulence, etc., can be at least partly explained by realizing that, if the ferment is produced by the bacteria, it may vary as the bacteria which produce it vary, and as they are changed by new conditions.
4. (1) Ferments are specific only in certain general ways, and it is plausible to assume the existence of a ferment which would act on the membrane of not only one species of bacteria, but on all bacterial membranes.  
(2) The solutions used as antigens contain bacterial protein in such finely divided form that these proteins may have been reduced to their component parts (for example, amino-acids), which are the same no matter from what proteins they are derived. The antigens have thus lost their specificity, and would naturally be the same. And still it is *not* certain that a staphylococcus "phage" is the same antigen as a colon one.
5. A number of observers have reported that they cannot repeat the experiment given as d'Herelle's argument "5." They maintain that the lytic substance is precipitated by alcohol, and that serial lysis can be initiated by this precipitate.
6. If the lytic substance were from bacteria, it would be foreign, and could be phagocytized.
7. In any case bacteria might be the source of the lytic substance.

**IV. THE LITERATURE**

Such in outline are some of the more important facts pertaining to the "bacteriophage," with the possible theories to explain them. The literature since 1915 consists of about 190 articles by some 80 authors. Of these authors, 35 have published largely in French journals; 10 in German; 8 in British; 8 in United States; and 8 in South American publications.

The more important of the original articles, and all the articles which deal with therapeutic trials, are listed in the Bibliography below. It is perhaps worth while to call especial attention to d'Herelle's 300-page monograph,<sup>1</sup> and the report in the *British Medical Journal*<sup>5</sup> of the meeting in Glasgow where papers were presented by Twort, d'Herelle, Bordet, Gratia, and others, giving their arguments for and against the "ultramicrobe" theory.

**V. THERAPEUTIC TESTS**

Convinced of the soundness of his theories and the therapeutic possibilities of his "phages," d'Herelle started practical experiments. He first worked on laboratory animals, and was able to immunize rabbits against a dose of Shiga and typhoid bacilli which killed controls in five days. He felt, however, that the crucial test was to treat "susceptible" animals for their own epidemic diseases.

He went, therefore, into an area where there was an epidemic of "chicken typhoid." The epidemic had raged for two months. Two-thirds of the fowl had died, and more were dying every day. Of those remaining, many were sick. To sick and well alike he gave 0.5 c.c. subcutaneously, or 1 c.c. by mouth, of a lytic solution active for the particular organism responsible for the disease. The result reported is that the sick recovered; no new cases developed; and all the fowl had active "phages" in the stools. The experiment was repeated in other places, with the same unfailing result. Often only one "yard" was treated and "saved," while in the yards around it the epidemic raged; or only a few individuals in a yard were inoculated, and these

few kept well while the others sickened. However, in a short time the uninoculated picked up the active "phages" and "caught immunity."

D'Herelle next went to Cochin-China, where there was an epidemic of hemorrhagic septicemia among the domestic buffalo. In one province where there were 30,000 buffalo, 10,000 had died. Ninety-nine per cent. of those infected died in eighteen to thirty-six hours. The etiologic organism was so virulent that 0.002 c.c. of a culture would kill an animal in about thirty-six hours. D'Herelle claims that by giving subcutaneously 0.04 c.c. of a phage solution active for the etiologic organism, and waiting four days for immunity to develop, the inoculated buffalo would withstand five fatal doses, while controls died. After sixty days the inoculated buffalo would withstand fifty fatal doses. The phages appeared in the stools following inoculation, but were quickly lost because the particular organism did not persist in the intestine, and its phage, therefore, could not live.

Very few other therapeutic experiments on animals are reported. Piorkowski,<sup>12</sup> however, has made an interesting observation on animals with streptococcus septicemia. He gave them 1 c.c. of an active filtrate, and found them free from streptococci in three weeks, while controls still harbored the organisms.

Kuttner<sup>8</sup> reports negative results in attempting to immunize rabbits against typhoid.

After successful trials with animals d'Herelle was ready to try out his substance on men. He first gave it to himself, and found that from 1 to 30 c.c. of a phage solution active for Shiga dysentery bacilli, if taken by mouth, or 1 to 5 c.c. if injected subcutaneously, gave absolutely no reaction. In twenty-four hours a phage for Shiga bacilli, resembling in every way the one used, was recovered from his stools, no matter whether it had been given by mouth or injected subcutaneously. Likewise, after injecting in various parts of the body phages active for plague, typhoid, and staphylococcus, phages exactly similar to the originals were recovered from the stools.

Bruynoghe and Maisin<sup>18</sup> report somewhat different results following the injection of a staphylococcus phage. They maintain that the reactions which follow these injections in every way simulate an infection of a mild degree. They give this as an argument for the living nature of the phage.

With the assurance that the substance would not injure normal men, d'Herelle started the treatment of dysentery cases. He recognized that there was still one possible danger, namely, that if the substance did actually dissolve a large number of Shiga bacilli within a short time, it might liberate a large amount of their very potent endotoxins and in this way do harm. In addition to this danger there was also the possibility that no good would result from the injection of the substance because the etiologic organism might be of a "resistant" type. This last difficulty d'Herelle realized fully, and he, therefore, recommends treatment at the earliest possible moment before the invading organisms have acquired resistance.

D'Herelle's results, together with all other therapeutic trials published to date (June 1, 1923), are given in summary below. Various French writers have promised the publication of detailed studies soon, but these are not yet available. In all cases treated the solution used was active for the etiologic organism unless otherwise stated:

1. *Shiga dysentery*—d'Herelle.<sup>1</sup>

*Seven* serious cases were treated.

They were having from five to twenty-five bloody stools a day.

Each case was given a single dose of 2 c.c. by mouth.

*Result:* Blood disappeared from stools in from one to two days.

Stools were formed in from one to six days.

Convalescence was established in two to three days.

2. *Typhoid fever*—Beckerich and Hauduroy.<sup>13</sup>

*Seven* cases were treated. All had positive blood-cultures forty-eight hours before treatment was started.

Cases 1 and 2—adults with moderately severe form of the disease.

Cases 3 and 4—adults with “ataxodynamic form, with marked myocardial involvement.”

Case 5—an infant with severe form of the disease.

Cases 6 and 7—infants with a very severe form.

*Doses given:*

Case 1—on the eighteenth day—given 2 c.c. by mouth.

Case 2—on the ninth day—given 2 c.c. by mouth.

Case 3—on the eighth day—given 2 c.c. by mouth.

Case 4—on the twentieth day—given 2 c.c. by mouth.

Case 5—on the twentieth day—given 2 c.c. by mouth and 1 c.c. subcutaneously.

Case 6—on the tenth day—given 5 c.c. by mouth and 1 c.c. subcutaneously.

Case 7—on the fourteenth day—given 5 c.c. by mouth and 1 c.c. subcutaneously.

*Results:* “Sudoral crisis” in all cases two hours after administration.

Cases 1 and 2—“defervescence” in forty-eight hours.

Cases 3 and 4—“defervescence” in forty-eight hours, but died later.

Case 5—“defervescence” and “permanent apyrexia” in forty-eight hours.

Cases 6 and 7—“defervescence and euphoria” in forty-eight hours.

**3. Paratyphoid B**—Beckerich and Hauduroy.<sup>13</sup>

*Two cases* in infants with positive blood-cultures. One case of average severity and the other grave.

*Dose:* 2 c.c. by mouth and 1 c.c. subcutaneously on the twenty-third and ninth days.

*Result:* “Permanent apyrexia” in forty-eight hours.

**4. Pyelitis and cystitis**—Beckerich and Hauduroy.<sup>14, 15</sup>

*Eleven cases* with *Bacillus coli* infections—8 adults and 3 children.

*Dose:* 0.75 to 2 c.c. subcutaneously; one to four injections given.

*Results:* Six cases—clinical cure and no bacilli in the urine.

One case—clinical cure, but bacilli still present.

One case—cure, but other therapy was used at the same time.

Three cases—no change.

5. *Pyelonephritis of pregnancy*—Courcoux.<sup>16</sup>

*One case.*

*Dose:* 15 c.c. directly into bladder; and also subcutaneous injections.

*Result:* Febrile reaction for forty-eight hours.

Then complete disappearance of symptoms.

6. "Anthrax or furunculosis"—Bruynoghe and Maisin.<sup>17</sup>

*Six cases.*

*Dose:* 0.5 to 2 c.c. injected locally.

*Result:* Moderate local and general febrile reaction. Practically complete disappearance of lesions in twenty-four to forty-eight hours.

7. "Abscesses, furunculosis, and anthrax"—Gratia.<sup>18</sup>

Details not given; but "notable acceleration of healing" reported.

8. *Infections with Staphylococcus aureus and albus, and enterococcus*—Beckerich and Hauduroy.<sup>14</sup>

Details not given, but results reported as similar to those of Bruynoghe and Maisin and Gratia.

9. *Cholera*—d'Herelle.<sup>1</sup>

*Three cases.*

*Dose:* 2 c.c. by mouth of a phage solution *active, not for cholera vibrios, but for Shiga bacilli.*

*Result:* 2 of the 3 treated cases lived, while the other 113 untreated cases died.

10. *Flexner dysentery*—Davison.<sup>20</sup>

*Twelve cases* aged two months to four years, 3 moderate cases and 9 severe.

*Dose:* 40 to 120 c.c. by mouth.

100 to 500 c.c. by nasal tube to stomach.

5 to 198 c.c. by rectum; often twice a day.

Each case received from one to ten doses.

*Result:* "Unable to observe the slightest benefit or harm."

11. *Shiga dysentery*—Friedemann.<sup>22</sup>  
Details not given.  
*Result:* "No therapeutic results in man."
12. *Shiga dysentery*—Otto, Munter, and Winkler.<sup>23</sup>  
Details not given.  
*Result:* Could not confirm d'Herelle's claims.

#### VI. DISCUSSION OF THERAPEUTIC POSSIBILITIES

The trials reported are, of course, too few, the details too scant, and the results too variable to allow us to draw any conclusions as to the possible place of "bacteriophaged" cultures in therapeutics. But, unless one is to cast aside as "faulty observation" a good deal of the work so far reported, he cannot fail to find some hope. Real dangers seem to be eliminated if the solution is properly prepared and aged. The local and general reactions that are reported are unimportant.

One's enthusiasm about the future possibilities will depend somewhat on his ideas of the nature of the bacteriolysant. If it is truly an ultramicroscopic bacterial *parasite*, much could be expected from it as a fully developed immunologic agent, introduced from the outside, and capable of attacking at once the pathogenic organisms.

But even if there is a justifiable skepticism in regard to the living nature of the "phage," this should not in itself rule out a careful therapeutic trial. A powerful *bacteriolysant* is undoubtedly present, and after injection or ingestion is said to appear in the stools. It is therefore conceivable that such a substance, whether derived from ultramicrobes or from bacteria, might be helpful in combating infections, especially intestinal infections. If at the same time such an agent is capable of stimulating the invading organisms to produce self-destructive *autolysins*, perhaps it would be even more helpful than as a parasite. In this later case it would give a new way of attacking infectious diseases. Certain vaccine treatments have as an aim the stimulation of the cells of the host to produce antibodies for the invading bacteria. The new "bacteriophage" prepara-

tions would aim to affect not the body cells, but the invading bacteria themselves, and to stimulate them to produce their own antibodies.

It is also possible that, since the development in the intestinal tract of the lytic substance for the etiologic organisms has been definitely proved, there might be other ways to encourage its production than the injection or ingestion of the lytic substance itself. There is a remote possibility that autolysis of the invading organisms takes place in the early convalescence from any infectious disease. Is it possible to hasten this lysis, and hence bring about early convalescence by giving the bacteria the *conditions* under which they best produce autolysins? For instance, in the test-tube lysins are produced only in an alkaline medium. Is this a possible argument for alkaline therapy in pneumonia, pyelitis, and other infectious diseases?

And, again, leaving out the lytic substance as itself an agent in treatment, there is still the possibility that the lysed solutions of bacteria may be useful as "vaccines" of dead bacteria. Such dissolved cultures would have the advantages of vaccines "killed without heat." Some authorities also claim that bacterial protein in finely divided form is more efficient as a stimulator of specific antibody formation than whole organisms. It is interesting to note in this connection that the phaged solutions have a high opsonic index, and that their injection into animals gives a serum containing agglutinins and amboceptors for the bacteria whose lysed solution was injected. It is perhaps significant that the two infections in which vaccines are most successful, namely, typhoid and staphylococcus, are the ones for which the best results with "phages" have been reported.

It is also possible that if vaccine therapy is to be looked upon as treatment by *non-specific* bacterial protein, this protein, so finely divided that it is reduced to the elements common to all bacterial protein, might have advantages. D'Herelle's 2 cases of cholera treated with a Shiga phage are interesting in this regard.

A final application of the "bacteriophage" phenomena is suggested by the selection of "resistant" organisms. Is it pos-

sible that vaccines made in the ordinary way but using only these especially virulent strains would be more effective?

#### VII. LABORATORY DIFFICULTIES

The preparation of lytic solutions requires only ordinary bacteriologic equipment and a Berkefeld filter. It requires more than ordinary care in the preparation of media and in carrying through the details of the technic. But no matter how great the care, it is by no means as easy to get results as the foregoing reports would seem to indicate. For instance, it is much more complicated than running a sample of tap-water through a Berkefeld filter, and adding the filtrate to a typhoid culture. In fact, the careful handling of a great many specimens of stools, pus, etc., may yield no lytic substance, or else give one that is so weak that it could never have therapeutic value. Vaccine preparation is very much simpler than the preparation of "phages." Therapeutic application of the lytic solutions is, therefore, complicated by laboratory difficulties. The apparent ease with which the French observers get very powerful lysants makes one wonder if their media is more suitable for the development of phages than the media as ordinarily prepared in this country.

#### VIII. SUMMARY

1. Twort, d'Herelle, and others have demonstrated a new phenomenon of "transmissible bacterial lysis."
2. The lytic substance does not act uniformly throughout a culture, but seems to concentrate its action in certain spots.
3. It can separate or change a "pure culture" of bacteria into sensitive, "lysogenic," resistant, and other forms.
4. The substance can be obtained from various body excretions, secretions, and tissues; as well as bacterial cultures, earth, sewage, and water.
5. It keeps indefinitely under proper conditions, and resists heat to 75° C. It is sensitive to quinin and glycerin, and is probably precipitated by alcohol.
6. It is non-specific in its action, although at first it acts

only on a particular group of organisms. Its "virulence" for a given organism can be increased, and it can acquire "virulence" for organisms of the same or different groups. Up to the present time about twelve groups of bacteria pathogenic for man have been affected.

7. The substance will act only on relatively small numbers of young, living organisms, in an alkaline medium.

8. A series of experiments seem to prove that it is "corpuscular" in nature.

9. Microscopic and ultramicroscopic observations are of interest.

10. The blood from animals injected with the lytic substance contains antilysins; and an amoebaeceptor which some authorities say will fix complement with any lysed bacterial solution as antigen.

11. Lytic substances are present in normal stools, and throughout the course of an infectious disease; but they are not active for the etiologic organism until convalescence.

12. After subcutaneous injection the lytic substance is said to appear in the stools.

13. In animal epidemics the substance can be transferred from one individual to another.

14. Remarkable preventive and therapeutic results in animals are reported by d'Herelle.

15. French observers report good results in the treatment of typhoid, dysentery, and pus infections in men.

16. American and German observers have failed to confirm these observations.

17. D'Herelle's explanation of the new bacterial phenomena is that they are brought about by living ultramicrobes which are normally parasitic on intestinal bacteria, but, in disease, acquire "virulence" for pathogenic varieties.

18. Bordet and others hold that the phenomena can be explained by assuming that the bacteria themselves, under certain conditions, produce autolysins.

### IX. CONCLUSIONS

1. The nature of the new lytic substance is not yet known. No crucial experiment has been devised. The evidence for its being an autolytic ferment seems to be increasing, but no one has proved that it is not a living organism.
2. Whatever its nature, it may have therapeutic possibilities either as
  - (1) A parasite on bacteria;
  - (2) A ferment which will lyse bacteria, or stimulate them to autolysis; or
  - (3) A vaccine acting on the cells of the host.
3. The therapeutic trials, up to the present, are few and contradictory, but they offer some hope in the treatment of certain infections for which we can at present do little.

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MODERN DIAGNOSIS OF DISEASES OF THE GALL-BLADDER

THE frequency of gall-bladder disease must be emphasized. It is well known that 5 to 12 per cent. of all women coming to autopsy have gall-stones, and if younger women are excluded the percentage is higher still. In addition, there must be a much larger group of men and women in the country who have acute or chronic disease of the gall-bladder which has not reached the stage of stone formation. When we consider these figures we are forced to the conclusion that the careful clinician and family doctor are not making the diagnosis of gall-bladder disease often enough, and that many cases must be overlooked.

This happens because the diagnostic symptoms, signs, laboratory findings, and x-ray data are notoriously insufficient in many cases. Typical colics are few. Jaundice is only found in a small percentage of the cases. Laboratory findings have been almost absent till recently, and x-ray technic is just reaching the stage where it is important in diagnosis. Positive findings all along the line have real value. Negative findings do not rule out disease of the gall-bladder.

It simplifies our conception and diagnosis of chronic disease of the gall-bladder to include cases with and without stones in one large group, and to think of them as earlier and later stages of the same process with stones as a frequent complication of many of the late cases.

There is nothing new in the last few years in history taking or ordinary physical examination, but there has been a determined

effort to improve our diagnosis by collecting the bile through a duodenal tube, and examining it in diseases of the liver just as we examine the urine in diseases of the kidney; also the x-ray examination is steadily growing in importance, and is often valuable and quite often decisive. In reviewing the subject we shall touch briefly on the history and ordinary physical examination, and take up more fully the newer examination by biliary drainage and the x-ray.

**The History.**—This may be characteristic, but more frequently is not. We have several types of cases, those with typical colics, those with moderate local grumbling pain or soreness, and those with vague indigestion without local symptoms.

Typical colics are few, with sharp pain in the liver region running around the right side and up into the right shoulder, and vomiting during attacks of pain. Such cases often have large stones and a contracted gall-bladder, but the pain may be just as severe in chronic cholecystitis from spasm or infection of the gall-bladder as in cases with stones. The doctor must remember that *recurring* attacks of severe pain which may waken the patient at night and leave the upper abdomen sore for several days are usually due to organic disease, and cannot be explained by "ptomain poisoning," or acute indigestion, or a neurosis. In most gall-bladder cases we have the past history of attacks of "acute indigestion." It is surprising how often this diagnosis is still made.

The severity of the pain is unlike the average gastric or duodenal ulcer and cannot be relieved by alkalies or atropin, but requires morphin. The pain is not referred in a constant way. In some it is local and not referred at all; in some it is typically referred around the right side and to the right shoulder; in others, straight through to the back, and in a few, to the left shoulder.

The group of gall-bladder cases with local grumbling symptoms is a much larger one. Here we often find a thick old gall-bladder and cystic duct obstruction with or without stones. The patients have soreness or a constant ache in the right side,

which is often made worse by exercise. The distress or heartburn is usually irregular, with little relation to meals or time of day or night, unlike the usual ulcer hunger-pain or distress. Occasionally we find a typical "hyperacidity" in a gall-bladder case which is relieved (but not cured) by the usual alkali and frequent feeding plan used in ulcer. This therapeutic test is often valuable in diagnosis. The "hyperacidity" and x-ray deformity in the region of the duodenal bulb (from adhesions) may lead to the diagnosis of probable ulcer, but the poor result of systematic ulcer treatment makes one suspect that the gall-bladder, not duodenal ulcer, is the actual cause of symptoms.

The largest group of gall-bladder cases and at the same time the most difficult to diagnose are those with vague indigestion without local symptoms. They complain chiefly of belching and distress. They feel "bilious," but rarely are jaundiced. Nausea, regurgitation of food, and heartburn are common. They masquerade as intestinal indigestion and gastric neurosis. This type of gall-bladder symptoms is most common in fat, soft, sedentary women of middle age, though others may have them.

A previous history of infection, such as typhoid, sinusitis, tonsillitis, tooth abscess, or influenza is useful, because such things often leave a damaged gall-bladder. Fever or chill shows active infection. Fever may be absent in cholangitis in weak people.

Jaundice is a very valuable sign when present. Unfortunately for diagnosis it is very frequently absent. Surgical statistics sometimes give very high figures for jaundice—even 20 or 30 per cent. This is true only for the severe, chronic cases coming to operation, not for the whole group of gall-bladder cases, early and late, in which 5 or 10 per cent. would probably represent the incidence of jaundice. There is a danger in these high surgical figures. They make jaundice appear a common and important sign, and they help us to overlook the far more abundant early "medical" gall-bladder cases without jaundice. Rapid development of jaundice after pain favors stones, two or three days later catarrh. Slow, progressive jaundice occurs

in either cancer or stones. Variability of jaundice favors stones. The fact that jaundice is more common with stones than without helps little in the diagnosis of the individual case, but this is unimportant because treatment depends largely on the severity and duration of symptoms, not on the presence or absence of stones.

It is better to give most painless jaundice cases in middle life the benefit of an exploration, and not dismiss them as probable cancer. Some cases may prove to be impacted stone and curable by operation. In painless jaundice of even four to six weeks' duration it is wise to consider the occasional *possibility* of the rare disease—acute yellow atrophy of the liver. This is not always as acute as its name implies. I have seen 2 recent cases proved by autopsy in which the jaundice lasted for one or two months.

**Physical Signs.**—The patient is often a woman of forty to sixty-five, though with greater care and skill we shall recognize cholecystitis more and more in the twenties and thirties, when the trouble begins. We may or may not have local tenderness or resistance over the gall-bladder. Spasm may be absent in chronic cases, with serious inflammation or even gangrene. Putting the patient in a left lateral position helps to bring the liver down where it can be felt (just as a right lateral position does the spleen). The gall-bladder itself is palpable in only 1 or 2 per cent. of cases. It is usually out of reach up under the liver unless decidedly enlarged. In a large percentage of the cases with stones the gall-bladder is smaller than normal. In rare cases, notably with stone in the cystic duct, the gall-bladder becomes much distended with light colored bile and mucus, and is easily palpable.

There is nothing distinctive about the gastric contents. Secretion is frequently normal or low, sometimes absent; in a small group of cases there is high secretion from reflex irritation. The urine is bile colored and the feces are clay colored and fatty in obstructive jaundiced cases. Variability in the color favors stone, as against cancer. Occult or gross blood in the stools is more common in peptic ulcer than in gall-bladder disease,

but, unfortunately for diagnosis, is occasionally found in gall-stone cases even without jaundice.

*Cholesterol.*—Since gall-stones are largely composed of cholesterol, it is natural to expect an increase in the cholesterol in the blood, and it was hoped that such an increase might prove a diagnostic point. Unfortunately for diagnosis increased cholesterol in the blood is found in many other conditions, such as, arteriosclerosis, nephritis, diabetes, skin diseases, cancer, pregnancy, etc., and even in a gall-stone case the period of stone formation may be so long previous that normal blood cholesterin is found when the test is made. For these reasons cholesterol blood tests have not proved of much use in diagnosis.

**The x-Ray Examination.**—The time has come when it is no longer fair to dismiss the x-ray examination of the gall-bladder with a few brief and disparaging remarks, as is still done in some recent text-books and medical papers. It is easy to understand this attitude. There have been many disappointments. The doctor has received many negative x-ray reports. The plates, perhaps poor, perhaps good, have shown nothing when gall-bladder disease was present. This may happen so many times that confidence in the method is entirely lost. Unfortunately, most of the diseased gall-bladders are free from stones, and many are so thin walled that they will not show on the plate, and, in addition, many stones are too soft to throw a shadow. It is one more example of negative findings not ruling out gall-bladder disease. In looking over hundreds of gall-bladder plates each year from my own and other laboratories, I realize how many are taken which show nothing, so many that hospitals especially are inclined to let their gall-bladder work drop into the background.

However, there is another side to this picture, the technic has developed rapidly of late, and is steadily giving us more evidence of chronic gall-bladder disease, which can and does help greatly in diagnosis in several ways. *First*, the x-ray examination may exclude the presence of other organic lesions, such as ulcers and cancers, changes in the appendix, etc. *Second*, it often shows shadows of stones or the thickened or enlarged

gall-bladder on the plate. *Third*, it may give indirect evidence of pressure and adhesions starting from the gall-bladder, and involving the stomach, duodenum, jejunum, or colon.

Some of this evidence is clear and absolutely decisive, for example, the clear picture of unmistakable stones may alone make the diagnosis in an obscure case. Some of it is suspicious or suggestive, for example, faint or doubtful stones, or slight adhesions in the gall-bladder region; and some of it is very doubtful, possibly misleading, such as vague shadows, small areas of density in the gall-bladder region, possibly due to food or drugs, which one man will call suspicious, and another not.

In short, we run the gamut of diagnostic, suggestive, and doubtful evidence in *x-ray* work as in any physical examination, but in spite of doubtful results there remains a large group of gall-bladder cases in which the *x-ray* has been of very great help in diagnosis. I can point to scores of such cases in my own experience in the last few years, and now insist on several gall-bladder plates in practically every chronic digestive case which comes for examination.

Very much depends on *x-ray* technic, the care, the thoroughness, the enthusiasm of the roentgenologist, and last, but not least, the interpretation of plates needs great skill and experience and a level head, in order to see all, but not too much, in the plates. If anything is worse than missing a gall-stone, it is to see one that does not exist and advise operation therefor.

The results in a hurried hospital routine, with old screens and patients who do not understand and do not hold their breath, will always fall far below the best results obtainable in a private laboratory.

*The x-Ray Evidence.*—Now we turn to the evidence, remembering that positive is much better than negative, and that we never hesitate to make a diagnosis of gall-bladder disease with a clear history even if the *x-ray* examination shows nothing. The evidence varies in kind and importance.

*Direct evidence* consists of (1) pictures of the stones themselves (Figs. 135-143), single or faceted, often ring shaped, found in the gall-bladder region and moving on respiration or

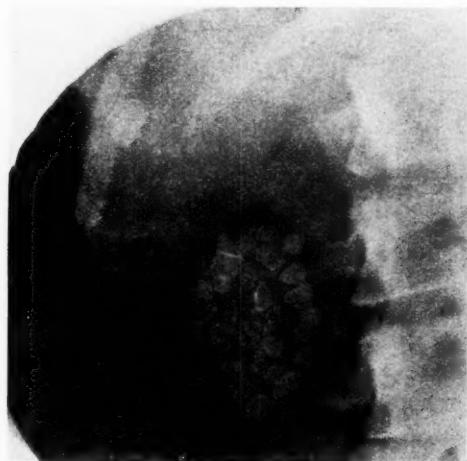


Fig. 135.—A large number of gall-stones of rather dense type.



Fig. 136.—Single dense gall-stone.



Fig. 137.—Gall-bladder containing seven large dense faceted stones. Traces of barium in hepatic flexure.



Fig. 138.—Group of small irregular gall-stones. Liver edge and kidney outline are seen.

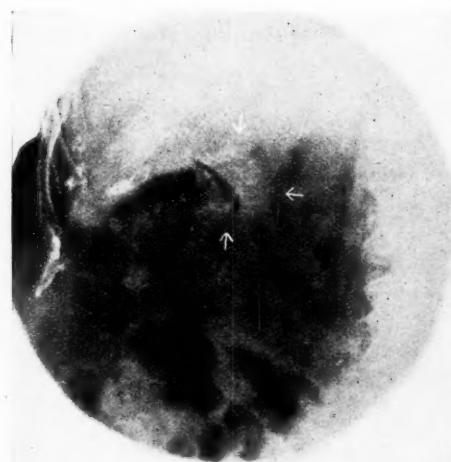


Fig. 139.—Round, somewhat contracted gall-bladder filled with very small bilirubin lime stones.



Fig. 140.—Group of small stones just above hepatic flexure filled with barium.



Fig. 141.—Narrow gall-bladder filled with pea-sized ring-shaped stones.  
Barium in hepatic flexure is seen below.



Fig. 142.—Three faint ring-shaped gall-stones, showing relation to stomach.

change of position with the liver or gall-bladder, not with the kidney. These stones are rarely confused with kidney stones or calcified glands on account of their shape, density, structure, mobility, and position. The stones usually cast a positive, rarely a negative shadow, according as they are more or less dense than the surrounding bile. (2) A dense or enlarged gall-bladder often overlying the upper pole of the right kidney, but occasionally more to the right or larger or lower, depending on the size of the gall-bladder and position of the liver (Figs.



Fig. 143.—Single gall-stone patient has pancreatitis and mild diabetes.

144-147). The abnormal gall-bladder casts a shadow because of a very thick wall, or because of increased density of its contents, thick bile, fine sand, etc.

*Indirect evidence* consists of adhesions which (1) pull the stomach to the right and perhaps deform the antrum or pyloric region (Figs. 148, 149). (2) Adhesions which deform the first and second portion of the duodenum. This deformity may be slight or very marked and striking (Figs. 150-153). (3) Adhesions may hold the coils of jejunum up in the right upper quadrant; this is not very common, but is interesting when it occurs. (4) Adhesions may lift or hold up the hepatic flexure



Fig. 144.—Small rounded gall-bladder filled with dense, tarry bile and fine sand. The liver edge and kidney outline are clearly shown.



Fig. 145.—Rounded pole of gall-bladder outlined by small stones and fine sand.



Fig. 146.—Large dense gall-bladder overlying upper third of right kidney.



Fig. 147.—Rounded gall-bladder outline overlying right kidney. Note kidney outline and hilus of right kidney just to right of the pole of the gall-bladder.

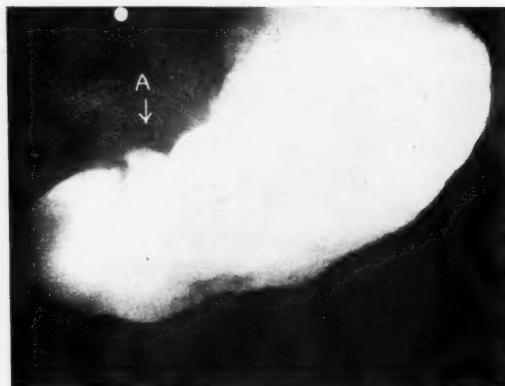


Fig. 148.—Subhepatic fixation of antrum by gall-bladder adhesions. Duodenal cap, A, lies close to the lesser curvature.



Fig. 149.—Antrum pulled to right by gall-bladder adhesions which deform antrum and duodenal cap.



Fig. 150.—Second portion of duodenum pulled far to right by gall-bladder adhesions; deformity of duodenal cap resembles ulcer.



Fig. 151.—Peculiar deformity of duodenal cap produced by gall-bladder adhesions; the first portion of the duodenum is dilated and pulled to the right and bent downward.



Fig. 152.—Gall-bladder adhesions deform the first and second portions of the duodenum. The gall-stones in this case are shown in Fig. 138.



Fig. 153.—Subhepatic fixation of antrum and deformity of first portion of the duodenum produced by gall-bladder adhesions.

in the gall-bladder region. (5) The first or second portions of the duodenum or the hepatic flexure may show the smooth rounded pressure of an enlarged or pathologic gall-bladder (Fig. 154). The theory is that a normal gall-bladder is too soft to produce this kind of pressure deformity.

(6) Secondary spastic changes in the stomach have some importance in diagnosis. There is a tubular spasm of the an-



Fig. 154.—Pressure of pathologic gall-bladder upon large atonic first portion of the duodenum.

trum (Fig. 155), which is quite characteristic of a chronic gall-bladder.

(7) George and Leonard have stressed the presence of barium in the ampulla of Vater as a useful sign of gall-bladder disease. It is not common, but in their experience it is never found in normal persons. Every case showing it which has come to operation has had a chronic gall-bladder.

The importance of the different kinds of *x*-ray evidence may

be placed in the following order: (1) A clear, unmistakable stone or stones found in the gall-bladder region. This is perhaps the only *positive* x-ray evidence of a chronic gall-bladder. (2) A clear, dense, or enlarged gall-bladder often overlying the upper pole of the right kidney. There is considerable discussion at present whether the normal gall-bladder will cast a shadow or only the diseased ones. I believe that practically all bladders which show on the x-ray plate with our present-day technic are abnormal, but that occasionally a normal gall-bladder will



Fig. 155.—Tubular spasm of the antrum due to pathologic gall-bladder.

also show when the liver is thin and the gall-bladder projects below it. (3) Next come the deformities in the right upper quadrant due to adhesions and spasm, the fixation and deformity of duodenum and stomach, and, less commonly, of colon and jejunum. They are valuable evidence, but we must use great care in diagnosing a chronic gall-bladder infection from adhesions or spasm alone, as there are other causes in the right upper quadrant, notably peptic ulcer or even the appendix. Of course, we may have chronic cholecystitis *without* such adhesions involving the stomach or bowel.

Be sure that the roentgenologist who reports the stomach *pulled* to the right side (by gall-bladder adhesions) has examined the patient in the erect as well as the prone position, and has used the fluoroscope as well as plates. It is surprising to see where the stomach will occasionally go when the patient lies down on it. It may slip or be squeezed over to the right side, and look as if *pulled* over. We occasionally see right-sided stomachs in prone plates which are median and freely mobile when the patient is erect. It is very important to take all this indirect evidence as corroborative only, and not urge operation on this ground alone, but with the clinical history plus these findings. (4) Last in importance come the doubtful stones, hazy gall-bladder shadows and slight adhesions; with improved technic these difficulties may increase, more is seen in the right upper quadrant and interpretation is harder. We get pictures of food remains in the duodenum or small intestine, bismuth given by mouth for treatment, as well as mesenteric and other glands. In this group most positive mistakes are made, and stones and thickened gall-bladders are diagnosed which do not exist.

Patients should not be sent to the roentgenologist "for gall-bladder plates" alone. These should always be part of a general gastro-intestinal or abdominal examination, otherwise ulcer or cancer or the appendix may be overlooked. Besides this, a completely negative gastro-intestinal examination in a patient with important digestive symptoms often makes one suspect the gall-bladder.

*Statistics.*—How often will the *x-ray* examination show evidence of chronic gall-bladder (not gall-stones alone, but a chronic cholecystitis with or without stones)? Statistics are very unsatisfactory here, and often misapplied. First, we must distinguish between (A) *all cases examined* and (B) *all cases operated*.

(A) What percentage of chronic gall-bladders are found in all cases examined, and what percentage are missed? No one knows. We never can get statistics on the total group.

(B) What percentage of chronic gall-bladders are found in

the operated group? Here statistics are few, for most roentgenologists have published only the percentage of *stones* found in their operated group.

The percentage of stones found in the operated group runs from 10 to 15 per cent., with poor technic, to 50 or 60 per cent. with the finest technic—greatest care and expense (skilled operators, fresh screens, abundant plates, etc.).

When we add to this positive evidence of stones all the other evidence of a pathologic gall-bladder, such as gall-bladder shadows, adhesions in the gall-bladder region, and signs of pressure of the gall-bladder upon the stomach, duodenum, or colon, we increase the positive *x-ray* diagnosis much more; so that it may even occasionally reach 90 per cent. in a brilliant series of operated cases (Kirklin). Herein lies the importance and value of the *x-ray* examination of the gall-bladder.

It is a common fallacy to unconsciously *apply these high percentages of positive diagnoses to gall-bladder cases as a whole*, and to forget that they only apply to the operated group, namely, to the latest, most serious, and most definite cases, the cases with the most positive evidence of all kinds. It reminds one of the surgeon who talks about peptic ulcer and forgets that the only group he sees is a small selected group of the most difficult and dangerous ulcers, which have resisted medical treatment.

Now let us turn to the far larger and less definite group of gall-bladder cases which do not come to operation. What about the gall-stone cases? We have no statistics. Furthermore, what about the larger group of subacute and chronic cholecystitis cases without stones? We have no statistics here, perhaps we shall have in the future. Our strong impression is that it is impossible to show the majority of chronic gall-bladders without stones by *x-ray* examination at present, but at the same time by using all the direct and indirect evidence at our disposal an important group of cases are discovered, and in a large *x-ray* clinic the number of such cases correctly diagnosed is imposing, even though the actual percentage found is probably far lower than the figures given above for the operated group.

It has been found in some clinics that in cases with a negative x-ray report of the gall-bladder, and where the barium examination has shown *no other lesion*, no gastric or duodenal ulcer or cancer, no appendix or surgical disease of the colon, and yet with symptoms severe enough to demand a laparotomy, that many chronic infected gall-bladders are found. In short, a negative barium examination in a patient with severe digestive symptoms requiring operation casts a strong suspicion on the gall-bladder.

**Biliary Drainage.**—The Meltzer-Lyon drainage of the bile-passages gives us bile to examine in disease of the gall-bladder and liver much as we examine urine in diseases of the kidney. It is the latest and most elaborate laboratory method we have ever had in diseases of the gall-bladder. It has attracted much attention and has been tried in clinics throughout the country for the last two or three years, and we now have a large amount of data on which to form an opinion of its value.

The appeal of the method is strong to both doctor and patient. The doctor has some of the contents of the bile-passages in his hands after a fairly simple procedure, and can examine it in any way he chooses in the hope of early and better diagnosis and early preventive treatment. The "biliary" patient sees his bile taken out of him, and feels that he is cleaned out and something nasty taken away.

There is much that is easy about the method. It is easy to get the patient to submit to it in the hope of better diagnosis and medical cure. It is easy to get the tube in; in 100 consecutive ambulatory cases the position of the tube was verified by the fluoroscope, and showed that 80 were in the duodenum in twenty to thirty minutes, 15 in one-half to one hour, 1 in two hours, and 4 failed to pass. In the sicker cases the failure to pass the tube into the duodenum may reach 10 per cent. It is easy to get the bile out. Anyone can do it, a nurse or attendant, or even the patient himself with a little training.

On the other hand, it is *not* easy to tell just where the bile comes from, or why it flows so freely, or to explain exactly the color changes in the bile, or to decide about the cells one sees,

whether they come from inside the bile-passages or from outside (stomach, duodenum, etc.), or whether or not the bacteria are causal or merely contaminations. It is not easy to estimate its diagnostic value in a large series with few operations.

*Physiology.*—A brief summary of the physiology of the method is important. Magnesium sulphate introduced into the duodenum relaxes the sphincter at the end of the common bile-duct, and Meltzer suggested that the activities of the sphincter and gall-bladder must be co-ordinated if the contents of the gall-bladder are to be forced into the bowel, and the magnesium sulphate when it relaxes the sphincter must cause a reflex contraction of the gall-bladder, much as urine is passed by relaxing the bladder sphincter and contracting the bladder.

Meltzer's theory of contrary innervation as applied to the gall-bladder has been somewhat discredited by finding that many other substances beside magnesium sulphate will produce a typical bile flow when injected into the duodenum, and as most of these drugs do not relax the sphincter, it cannot be assumed that they reflexly stimulate the gall-bladder; a bile flow can also be obtained without using drugs at all. The gall-bladder is a limp and sluggish organ, and never contracts like the urinary bladder, and the evidence to date suggests that the bile flows chiefly because the pressure in the common duct has been lowered by relaxing the sphincter at the lower end. We are often in doubt how much the gall-bladder has emptied in the individual case. The gall-bladder is evidently a storage reservoir for the smaller continuous secretion of the liver, and this storage capacity is increased by its great power of concentrating the bile. In addition, it acts as a pressure equalizer for the bile-passages.

The bile flow is usually light yellow at first, later changing to darker yellow, and later still to light yellow again. Lyon's theory is that the first pale yellow or "A" bile comes from the common duct, that the second darker "B" bile comes largely from the gall-bladder, and the third clear yellow "C" bile is freshly secreted liver bile; thus he believes that we are able to obtain the bile *separately* from the common duct, gall-bladder,

and liver, and establish a refined diagnosis of different sections of the biliary system.

Einhorn's theory that the darker bile is due to stimulation of liver secretion by the magnesium sulphate is directly controverted by Frazer's experiments at the Mayo Clinic with bile fistula dogs in which there was no change in the flow or color of the bile after introducing magnesium sulphate into the duodenum.

The practical point is that it is possible to empty the bile-passages more or less completely at will by the use of magnesium sulphate, and that this material is well worthy of study.

*Technic.*—This may be briefly described as follows: The patient is examined fasting, the teeth brushed, and mouth rinsed out. The sterile duodenal tube is passed into the stomach, the fasting contents aspirated, and the stomach washed clean with a weak zinc chlorid formalin solution.\* The patient then lies on a couch in the right lateral position, and swallows the tube slowly to about the 75 cm. mark, taking about twenty minutes. When the tube is in the duodenum (usually verified by fluoroscope), the duodenal contents are aspirated and the duodenum is doused with about 30 c.c. of a saturated solution of magnesium sulphate in water, mixed with 60 c.c. of water. Then gentle aspiration is begun and the bile flow is continued largely by siphonage. The actual drainage usually takes about thirty minutes and 15 or 20 c.c. of A, and 50 or 60 c.c. of B and C. bile obtained. Then the duodenum is doused with 300 c.c. of normal salt or Ringer's solution and the tube withdrawn.

The color, clearness, and consistency of the biles are noted, also cells and crystals, and they may be examined for bacteria by smears and cultures. All these examinations must be made at once, as colors change and cells are rapidly digested by the pancreatic ferment.

*Color Change, Segregation.*—The separation of the three biles depends largely on color and is only approximate. The B

\* The stock solution is: Formalin,  $\frac{1}{2}$  grain; zinc chlorid, 2 grains; boric acid, 10 grains; water, 1000 c.c. We use 25 c.c. in 250 c.c. water for lavage.

bile may be darker or more turbid than normal, or of different greens and browns, or there may be no color change or an entire absence of bile. The color change in normal B bile is probably due to the presence of bile which has been held back in the biliary passages by the common duct sphincter. The magnesium sulphate gives an increased flow of this stored bile by relaxing the common duct sphincter, and B bile is darker because there is *more bile* in the mixture of duodenal juices. It seems probable that B bile contains some gall-bladder bile at least, because it is concentrated, higher in bile salts (spectroscopic analysis), and we know that the gall-bladder concentrates the bile. Furthermore, B bile is absent, as a rule, when the gall-bladder is absent or filled with stones, and also in cystic duct obstruction.

It is interesting to see that in two severe surgical groups of gall-bladders we have 70 to 85 per cent. with no B bile (Cutler and Newton, Whipple) and only 30 per cent. with no B bile in a routine medical group (McCaskey). In the severe group there is frequent cystic duct obstruction preventing the emptying of the gall-bladder, or a gall-bladder full of stones so that no gall-bladder bile is obtained. The milder group has less pathology and little cystic duct obstruction and dark bile is usually found. In addition, the B bile commonly shows cells and crystals which are considered characteristic of gall-bladder contents and which closely resemble those found in the gall-bladder at operation. On the other hand, in experimental work, when dyes such as methyl blue (Crohn, Reiss, and Radin) or carmine red (Winkelstein) have been injected into the gall-bladder of animals, they have stayed there for days and it has not been possible to recover any by biliary drainage. It is difficult to reconcile these facts; possibly the anesthetic and operative procedures have upset the normal physiology in these experiments.

*Cells and Crystals.*—The examination of cells and crystals in the bile sediment has its difficulties. We see many extraneous (non-biliary) cells coming from the pharynx, stomach, duodenum, etc. Sometimes the result is like looking for a renal sediment

in a case of leukorrhea. Deep bile staining is usually seen in the true biliary sediments, leukocytes, and columnar epithelium from the ducts and gall-bladder. Whether abnormal cells come from the duodenum itself, or from the finer biliary ducts of the liver, or the larger ducts, or from the gall-bladder is sometimes difficult or impossible to determine. There is no question that many flocculi found in the B bile are the result of irritating the duodenal mucosa by the use of the hypertonic magnesium sulphate solution. They contain short columnar and cuboidal cells, leukocytes, bacteria, and mucus from the duodenum. Abundant cholesterol may suggest the possibility of stone formation. Occasionally a fine, gritty sediment of bile salts has been found in gall-stone cases.

Fitz in a recent study of 72 specimens of bile obtained directly from the gall-bladder at operation found the bile sediments rather disappointing for diagnosis. Pus-cells were more common in acute cases, epithelium and rare blood-cells in the chronic cases. Granular and crystalline débris was unimportant. There was very great variation of specific gravity, viscosity, and cholesterol. The cloudy biles usually came from acute gall-bladders.

*Cultures.*—The important bacteria most frequently found are in about this order: various streptococci, *Staphylococcus aureus*, the colon bacillus, and the typhoid bacillus; at least one-half the cultures are sterile or uncertain in chronic cases. The bacteriology is often unreliable and there is real difficulty in deciding whether the bacteria found are causal or accidental. More positive cultures are found in acute and subacute cholecystitis, and more sterile cultures in mild chronic cholecystitis and gall-stone cases. Occasionally the cultures are of great value, showing an abundant almost pure growth of pus organisms, which exactly match the organism found in some other focal infection, such as a tooth root, tonsil, or sinus.

*Diagnosis.*—The most important findings are:

1. Entire absence of bile in a proper drainage, which is found in common duct obstruction.
2. Absence of B or dark bile *on repeated tests*. In the more

serious cases this indicates some pathologic condition of the gall-bladder, cystic duct obstruction, a gall-bladder full of stones, very thick gall-bladder bile, or extensive adhesions about the gall-bladder. Absence of dark bile is quite often found in milder cases which are not operated, and its significance is doubtful at present. It may be attributed to poor emptying of the contents of the gall-bladder during the drainage.

3. B bile which is decidedly darker than normal in shades of dark brown to black indicates gall-bladder stasis.

4. A marked increase of leukocytes in the flocculi or sediment is found in inflammatory conditions of the passages. Tall columnar cells, often in fan or rosette formation, usually degenerated and deeply bile stained, and found in the B bile, suggest gall-bladder inflammation.

5. Sand or abundant crystals shows the presence of a tendency toward stone formation.

6. Abundant bacteria swarming or colonizing, shown by smears or cultures, have some real importance in cases of infection. In many cases the presence of bacteria have doubtful value on account of contamination from the mouth, throat, and stomach.

Positive evidence is far more valuable in diagnosis than negative, and indicates disease. By positive evidence we mean marked color changes, dark turbid bile, abundance of deeply bile-stained pus-cells and epithelium, abundant pure cultures of pathogenic bacteria, a sediment gritty with crystals, or such signs as complete absence of bile or entire lack of color change, no B bile, in repeated proper drainages.

It is impossible to tell at present just what percentage of gall-bladder cases show a definitely abnormal bile. It may be 50 per cent., it may be more. Negative evidence does not rule out disease, the chief pathologic area may be blocked off by cystic duct obstruction. Many chronic cases give sterile or insignificant cultures.

The more serious and active cholecystitis, cholangitis, and hepatitis cases prove the best group for diagnosis. If there is serious cystic duct obstruction, as in severe acute inflammation

of the gall-bladder, or some chronic fibrous cases, the bile drainage may show little, except the absence of B or darker bile. Occasionally in cholecystitis with much cystic duct obstruction a very small amount of gall-bladder bile is obtained, but this is so pathologic that a correct diagnosis can be made.

In gall-stone cases many give a normal or practically normal bile sediment probably because of cystic duct obstruction or because the gall-bladder is full of stones. The only suspicious feature is the absence of darker or B bile. We have seen several cases where gall-stones had been clearly shown by *x-ray*, and yet repeated drainages give nothing definite. Occasionally a great excess of crystals leads to a correct diagnosis of stones.

Cancers of the bile-passages are a difficult group for study. The drainage may easily fail on account of vomiting. The usual picture is entire absence of bile and perhaps of pancreatic ferment, with the presence of more or less blood.

*Summary.*—Some of the early interest and enthusiasm for biliary drainage has cooled as the limitations of the method are recognized, and an increasing number of cases checked by operation. The method has not realized all its original claims (few new methods do), and the question is asked in many clinics and laboratories whether or not the method is worth the trouble it takes.

It is difficult to estimate its total value at this time, although it has been in use for several years, and much has been written about it. There is much contradictory evidence at present, both clinical and experimental. The clinical papers are written almost entirely by those who have found the method useful in their own experience. Other trained men have tried it, have been disappointed, and have given it up, and their names do not appear in the literature, but I have found there are many such from personal interviews.

The physiology on which the method rests has been much questioned. While there is no doubt about the relaxation of the common duct sphincter by magnesium sulphate or the flow of bile after its use, there is considerable doubt about the contraction and degree of emptying of the gall-bladder.

An estimate of the value of the method in diagnosis is formed from two classes of cases, a smaller group of those operated, with a definite check on the method; a far larger group, not operated, in which we have no definite check. In the first, operated, group the method has shown up well in diagnosis, but, of course, these are, as a rule, the more serious or well-marked cases.

The second, non-operated, group are quite different. In these milder gall-bladder suspects the diagnostic details of color change, cells, crystals, and cultures may appear conclusive to one man and not to another. When this second group is very large in a reported series, say 80 per cent., and many are so-called "masked infections," with no definite symptoms or signs, except the evidence from bile drainage, we are on uncertain ground.

The method is somewhat elaborate and time consuming, with its intubation, lavage, aspiration, microscopy, cultures, repetition of the drainage, and often the use of the  $x$ -ray. There is difficulty in localizing the disease in the bile-passages. Many of the cells seen are evidently from the duodenum. A study of sediments from opened pathologic gall-bladders has proved disappointing for diagnosis. There is a minority of distinctive cultures and an abundance of colon bacilli and other bacteria of doubtful significance. The variety of opinions about the importance of color change, crystals, and cultures shows some uncertainty in the method at present.

On the other hand, biliary drainage has given us a definitely better diagnosis in a limited number of cases: (A) The inflammatory cases, acute cholecystitis and cholangitis, and acute exacerbations of chronic cholecystitis quite often show an abnormal bile thickened or darkened, with bile-stained epithelium, pus-cells, and mucus, and often positive cultures of the pus organisms or the colon bacillus. (B) No dark or B bile is usually found with a blocked cystic duct, a gall-bladder full of stones, or one which does not empty. (C) No bile is found in common duct obstruction (stones, cancer, etc.).

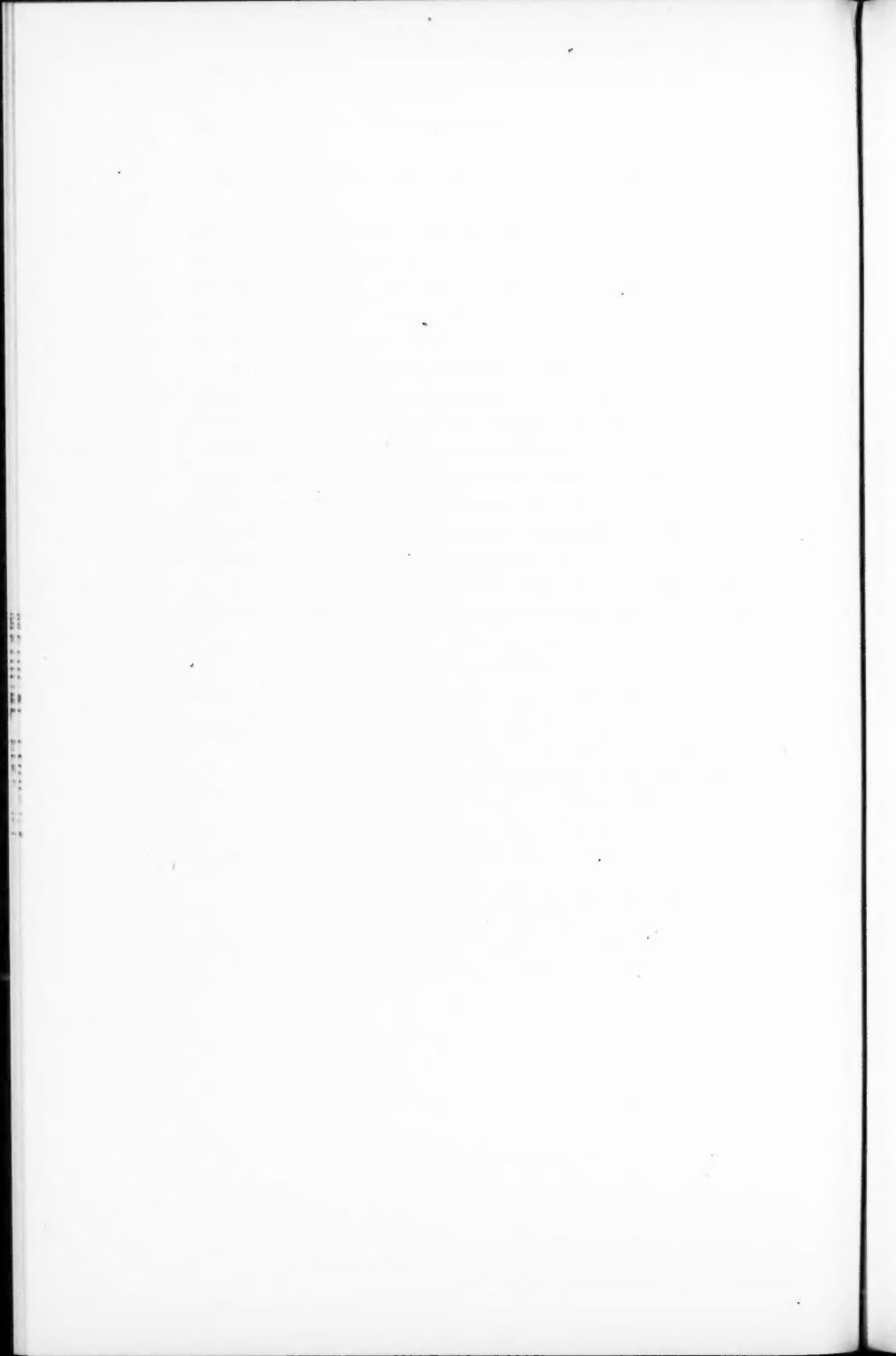
Clear bile with cultures usually sterile are found in normal

persons, gall-stone cases, and some cases of chronic cholecystitis.

We continue to use biliary drainage for diagnosis, realizing that its results fall far short of its early claims. We use it as part of our routine in addition to the history, the examination of the abdomen, and the use of the *x-ray*. We do not always expect to get a typical history of gall-bladder disease. We do not always expect to find a palpable tender gall-bladder on abdominal examination. We do not always expect to show a chronic gall-bladder on the *x-ray* plate. Neither do we expect a biliary drainage to always give positive returns, but we use it with the reasonable hope of getting diagnostic help in some cases, though not in all, probably not even in the majority, and with the object of using *all* diagnostic methods for all they are worth in the difficult field of gall-bladder diagnosis, and with the expectation that one method will supplement another, and by using all we shall get the greatest possible number of correct diagnoses.

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CLINIC OF DR. HUGO MELLA

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IRRADIATION OF THE THYMUS IN MYASTHENIA  
GRAVIS

In a search of the literature on myasthenia gravis a striking fact presents itself, namely, since Laquer and Weigert<sup>1</sup> in 1901 reported the finding of an abnormality of the thymus at autopsy in such a case, it appears reasonable to assume that it could not be a mere incident, as it has been observed by others. Bell<sup>2</sup> in 1917, in a review of the subject, states that at least 50 per cent. of the cases of myasthenia gravis coming to autopsy and reported since 1901 show either some enlargement or tumor of the thymus.

Timme,<sup>3</sup> in a discussion of Atwood's<sup>4</sup> case of myasthenia gravis, calls attention to the possible deficiencies in the internal glandular mechanism.

As the treatment of myasthenia gravis, in general, has been extremely unsatisfactory, the application of these necropsy observations by Pierchalla<sup>5</sup> is of considerable interest. Pierchalla reports the destruction of the thymus by use of the Roentgen ray in this syndrome with excellent clinical results.

The following 2 cases which came under my observation on the Neurological Service at the Massachusetts General Hospital, although by no means conclusive, are of enough value to be reported. The second case was reported at a meeting of the Boston Society of Psychiatry and Neurology on October 20, 1921.

CASE I

Out-patient record. February 20, 1920. Male, colored, age forty-eight, married; birthplace, Cape Verde Islands. Admitted to Throat Clinic. Complaint, increasing difficulty in

swallowing with present inability to swallow liquids; liquids regurgitate through nose when swallowing is attempted. Test drink of water given was expelled through nose.

**Physical Findings.**—Left nasal cavity: septum straight, inferior meatus wide, no pus, no polypi. Right nasal cavity: slight basal spur, inferior meatus roomy, no pus, no polypi. Posterior pharyngeal wall normal. Tonsils not seen. Vocal cords move normally. Slight edema of both arytenoids. Much frothy mucus in both pyriform sinuses. Limitation of movement of soft palate.

**x-Ray.**—Fluoroscopy: Liquids and semisolids met with a slight appearance of delay and showed a questionable irregularity at a point about opposite the level of the thyroid cartilage. No dilatation, and the delay was too brief to retain the barium long enough to take a plate. Some discomfort complained of when food passed this point. Evidence is not conclusive, but suggestive of a pathologic process in the upper third of the esophagus.

Referred to Medical Department for general examination. Pulse 68, temperature 98.5. Hemoglobin 85. Urine clear, reaction acid, specific gravity 1030, sugar negative, albumin negative. Well developed and nourished. Lungs clear. Heart, soft systolic murmur at aortic area. Abdomen negative. Knee-jerks present. Blood-pressure 140/105.

February 25, 1920: Referred to Neurological Department. Paralysis of palate—question cause. Says he cannot chew long, can work jaw up and down eight or ten times rapidly, then stops. No ptosis, no diplopia, no Rhomberg. Knee-jerks present and equal, ankle-jerks present and equal. Reaction of facial muscles to galvanism normal. Rapid fatigue of facial muscles to faradism. Diagnosis: Myasthenia gravis.

Marked purulent urethritis. Referred to Genito-urinary Department. Diagnosis: Gonorrhreal urethritis.

Patient did not return to the hospital until August 2, 1920, and was then admitted on the Neurological Service.

**Family History.**—Father died of "fever" at age of sixty-five. Mother died of smallpox at fifty. Mother had 15 children.

5 now living. No history of miscarriages, tuberculosis, cancer, or nerve disorder.

**Marital History.**—Married twenty-three years ago. Wife has had one child and no miscarriages. Has been here fifteen years and left wife in Cape Verde Islands.

**Occupational History.**—A laborer. Did building work up to one week before present illness, and the week just previous did work in a brass shop. Has not worked since last November (nine months).

**Social History.**—Lives with his married brother in Massachusetts.

**Past History.**—Always well and strong up to present illness. No history of accidents or operations. Admits gonorrhreal infection, but denies syphilis. Treated a few months ago at Massachusetts General Hospital for urethritis. Had smallpox in 1901. No other diseases.

Head: No history of aches, dizziness, or vomiting.

Eyes: Believes he has had diplopia during past two months.  
No eye-strain.

Ears: No deafness, tinnitus, or discharge.

Nose: No epistaxis.

Mouth: No sore throats.

**Cardiorespiratory:** No history of precordial pain, palpitation, edema, dyspnea, or orthopnea noted before present illness. No history of cough, night-sweats, hemoptysis, afternoon tire, or fever before present illness.

**Gastro-intestinal:** No sore mouth, nausea, vomiting, pyrosis, belching of gas, epigastric pain, no constipation, hemorrhoids, or jaundice.

**Genito-urinary:** Nocturia once or twice and dysuria during present illness. No history of hematuria, polyuria, retention, or incontinence. Acute urethritis noted above,

**Neuromuscular:** Negative before present illness.

**Skin:** Scarred from old smallpox.

**Habits:** Cigarettes, one package a week. Chews tobacco moderately, beer 3 or 4 glasses daily.

**Weight:** Believes he has lost 20 pounds in last year.

**Present Illness.**—Beginning nine months ago patient noticed increasing difficulty in swallowing, beginning with solid food and gradually applying also to liquid food. Foods and liquids regurgitated through the nose. Increasing weakness of the muscles of deglutition and chewing was discovered. Muscles of these groups tired quickly on use. Difficulty in speaking also was noticed by the family, the speech being normal for a while and then being very guttural and indistinguishable for periods of time and very labored. Difficulty in expectorating also was noted and general weakness of the arms and neck with considerable loss of weight were noted by the family.

**Physical Examination.**—A colored man of forty-eight with blackish-gray bristly hair, lying in bed in some discomfort and fairly restless, supported by head-rest. Some difficulty in breathing, but evidently more in keeping his mouth free from saliva because of difficulty in swallowing. Very thin and showing loss of weight.

*Head.*—Negative. Cheeks are hollow. Eyes: Sclera hazy, pupils fixed and small, equal. No nystagmus, fields of vision good by finger test. Nose: No obstruction, septum intact. Ears: Mastoid and sinus negative. Mouth: Teeth show considerable pyorrhea and are in rather poor condition. Cannot protrude tongue normally from mouth and cannot stick the tongue into either cheek. Soft palate reacts to touch rather sluggishly, but equally on both sides. Tonsils not seen.

*Chest.*—Fairly developed. Poor expansion. Breath sounds diminished over right upper lobe anteriorly. Voice sounds faint because of speech difficulty. A few crackling râles heard over right upper lobe at the back. Resonance slightly diminished over right upper lobe.

*Heart.*—Apex impulse not seen or heard. Heart sounds faint, regular, fair quality,  $A_2$  and  $P_2$  not accentuated. No murmurs, no thrill, pulses equal, regular, and synchronous. Radials slightly palpable, brachials slightly tortuous. Blood-pressure 134/104.

*Thymus.*—No evidence of enlargement on percussion.

*Spine.*—Negative.

*Abdomen.*—Sunken, soft, tympanitic. No masses, spasm or tenderness. Liver: Dulness fifth space to 3 cm. below C. M. on deep inspiration. Spleen and kidneys: Not felt. Abdominal reflexes absent.

*Genitals.*—Negative—no hernia. Cremasteric reflexes absent.

*Extremities.*—No edema, tremor, clubbing of fingers, shins negative.

*Reflexes.*—Biceps, triceps, supinator, and wrist-jerks present, active, and equal on both sides. Knee-jerks and patellar jerks equal and active. No Babinski, clonus, Oppenheim, or Kernig.

*Rectal.*—Not done.

All efforts of the patient to speak were made with considerable difficulty and lack of success in enunciating. Patient perspired considerably during the examination.

August 3, 1920: *Urine:* Color, normal clear; reaction, neutral; specific gravity, 1023; albumin negative; sugar negative; bile negative; diacetic acid negative. Sediment, rare white blood-cells and epithelium.

August 2, 1920: At 7 p. m. temperature 98° F., pulse 70, respiration 24. At 11 p. m. temperature 98.6° F., pulse 60, respiration 20.

August 3, 1920: At 7 a. m. temperature 98.4° F., pulse 58, respiration 20. At 3 p. m. temperature 97.6° F., pulse 62, respiration 24. At 7 p. m. 99.2° F., pulse 64, respiration 22. At 11 p. m. pulse 90, respiration 18.

**Summary.**—Patient of forty-eight years with history of progressive difficulty in swallowing, talking, chewing, and expectorating over period of nine months with considerable loss of weight due to inanition. The diagnosis seems to rest between myasthenia gravis and bulbar paralysis, the remissions of the symptoms favoring the former. There is also a question of esophageal tumor. (See O. P. D. x-ray report.)

August 3, 1920: Patient very weak and able to take but 14 ounces of fluids during day.

August 4, 1920: Failed rapidly around midnight, pulse growing weak and thready. Discharged dead at 1.03 a. m.

Final diagnosis: Myasthenia gravis.

August 4, 1920: Necropsy No. 4100; nine hours postmortem; John Silva, Nerve, No. 237.973, O. R.

*Anatomic Diagnosis:* Myasthenia gravis. Sarcoma of thymus. Congestion of the liver, spleen, and kidneys. Chronic pleuritis. Localized emphysema of lungs.

Clinical diagnosis on death report: Myasthenia gravis—bulbar type. Inanition.

The dead body of a man (mulatto), forty-eight years of age;  $165\frac{1}{2}$  cm. long, well developed, poorly nourished.

Head: On section the meninges are negative. Vessels of Willis, sinuses, and middle ears are negative. Brain weighs 1252 grams. The organ, outwardly, shows nothing definite except for some slight asymmetry of the medulla. The organ is preserved intact for microscopic examination.

Trunk: On section, subcutaneous fat is found in very small amount. Subcutaneous tissues are dry. Muscles negative, rather dry. Peritoneal cavity: No fluid. Appendix negative. Esophagus negative. Stomach: The mucosa is negative. Rugæ well marked. Pylorus negative. Small intestine: On section the mucosa shows some reddening along the first portion of the tube. Large intestine negative. Mesenteric glands: Show but little if any enlargement. On section, negative. Retroperitoneal glands negative. The anterior margin of the right lobe of the liver is at the costal border, in the right mammillary line. Diaphragm: Right, fifth rib. Left, fifth interspace. Pleural cavities: No fluid. Pleural adhesions: Right, fibrous adhesions posteriorly and to the diaphragm. Left, a few fibrous adhesions to the diaphragm. Thymus: In the situation of the thymus gland there is an ovoid mass  $7\frac{1}{2}$  cm. long,  $5\frac{1}{2}$  cm. wide,  $2\frac{1}{2}$  cm. thick. The mass is discrete. On section the tissue is plump, pale grayish white, quite firm, homogeneous, and lymphomatous-like. Thyroid gland is negative. Trachea and bronchi contain a moderate amount of pinkish semifluid mucous material. Bronchial glands negative.

Lungs: No area of consolidation. The tissue generally is spongy, pale red, and yields a moderate amount of thin reddish

frothy fluid. In the region of the apices and peripheral portion of the upper lobes there is quite a little frank emphysema.

Pericardium negative.

Heart weighs 240 grams. The myocardium is of good consistence, pale, brownish red. R. V. W. 3 mm., L. V. W. 10 mm. Columnae negative. Valve circumferences: Mitral,  $9\frac{1}{2}$  cm., aortic,  $6\frac{1}{2}$  cm., tricuspid,  $12\frac{1}{2}$  cm., pulmonary, 7 cm. The valves are negative. Coronaries are free, negative. Foramen ovale closed. Aorta and great branches negative. Pulmonary artery, veins, and venæ cavae negative.

Liver weighs 1064 grams, rather small. The capsule is smooth. On section the tissue shows a slight increase of consistence and is bloody. The section surfaces are brown and homogeneous.

Gall-bladder, bile-ducts: Negative.

Pancreas and duct of Wirsung: Negative.

Spleen weighs 90 grams; small. The capsule is smooth. The tissue is dark brownish red, elastic and bloody.

Adrenals negative.

Kidneys: Combined weight 223 grams; rather small. The capsules strip, leaving smooth, pale purplish-brown-red surfaces. On section the markings are retained. The cortex measures 5 mm. The tissue shows slight increase of consistence, and the section surfaces are purplish-brown-red and bloody.

Pelves, ureters, bladder, prostate, seminal vesicles, and testes: Negative.

**Bacteriologic Report.**—Culture on plain agar. *Heart:* Blood—no growth.

**Microscopic Examination.**—*Liver:* Negative. *Thyroid:* The follicles are rather large, have low epithelium and much colloid. *Hypophysis:* Negative. *Kidney:* Negative. *Adrenal:* No definite abnormality made out. *Spleen:* Much blood in pulp. *Thymus:* The organ is composed of a tissue rich in close-packed lymphocytes, through which bands of connective tissue extend. *Hassal bodies* are very few. Some of the nuclei of the lymphocytes are fragmented. *Myocardium:* There is possibly a very slight infiltration with lymphocytes in a few places.

**Report of Dr. James B. Ayer.**—Two sections of medulla removed: (1) through olives, (2) above crossing of pyramids. No abnormality noted in gross.

Microscopic examination shows no lesions of note in blood-vessels, a few lymphocytes in the perivascular sheaths are seen. There is no meningeal reaction either acute or chronic. The ependyma of the ventricle and of the upper spinal canal is normal and there is no subependymal gliosis. The choroid plexus is normal.

There is no exudate or evidence of chronic inflammation in the parenchyma of medulla and no neurologic changes of note. The cells of the XII nucleus and those of the vestibular nucleus appear, for the most part, normal. A few cells do show early degenerative changes, but this is the exception. The cells of the olfactory nucleus do not stain normally, but no evidence of pathologic change is seen in these sections.

#### CASE II

Out-patient Department. January 27, 1920. Female, white, age twenty-three, single; birthplace Russia; occupation saleswoman; residence Massachusetts.

Complains of difficulty with swallowing; this is more marked at times. Muscles of mastication and swallowing tire quickly and food regurgitates through nose. Voice becomes thick, then fails entirely after a few minutes of talking. This trouble was first noticed in July, 1919, and during the last three months has had to use finger to get food from cheeks. Lacrimation has been so severe that she had to give up sewing. Has felt very tired since the onset of the illness.

**Physical Examination.**—Bilateral ptosis more noticeable on left. Pupils are equal and react to light and distance. Palate reflex not obtained. Speech labored and not easily understood. Knee-jerks present and equal. Question of myasthenia gravis.

February 24, 1920: Still has difficulty in swallowing and speaking. Admitted to hospital for further study.

February 27, 1920: Well developed and nourished. *Skin:* Dry and clear. *Mucous membranes:* Pale, unable to show teeth

or to wrinkle forehead, mask-like face. *Eyes:* Marked diplopia. Bilateral ptosis of eyelids. Pupils react to light and distance. *Ears:* No deafness. No evidence of sinus or mastoid involvement. *Nose:* Negative. *Mouth:* Dentition good; no pyorrhea or lead-line, many fillings apparently in good condition. *Tongue:* Protruded in midline with slight tremor. *Pharynx:* Filled with saliva. *Tonsils:* Negative.

*Neck:* Thyroid negative. No glands palpable.

*Chest:* Well developed. Expansion equal on both sides. Breasts clear, no masses. *Heart and Lungs:* Negative. *Blood-pressure:* Systolic 116, diastolic 80. Brachials not tortuous.

*Abdomen:* Level, soft and tympanitic. No masses, spasm, or tenderness. *Liver:* Dulness fourth rib to costal margin. *Spleen and Kidneys:* Negative. *Genitals:* Negative. No hernia.

*Extremities:* No tremors, clubbed fingers, or edema. Shins normal. Knee-jerks present and equal. Ankle-jerks present and equal. No ankle-clonus. Plantars normal. No Kernig.

*Urine:* Normal color, reaction acid, specific gravity 1022. Negative for albumin and sugar.

*Blood:* White count 10,000. Hemoglobin 80 per cent. Smear negative. Non-protein nitrogen 117 per cent. Blood-sugar 31.8 per 100 c.c. Wassermann negative.

March 6, 1920: Out-patient Department.

Muscles of hands fatigue rapidly to faradism. Typical myasthenic reaction. Nuclein of thymus, gr. 1 t. i. d.

March 13, 1920: Feels very tired.

May 1, 1920: In same condition. Patient is going to country (rural district) for a short while. Continue nuclein of thymus.

July 1, 1920: Thinks she has more difficulty in swallowing. Liquids do not regurgitate through the nose. Dizziness on getting up quickly. No ringing in the ears. The fundi are normal.

August 31, 1920: *x*-Ray report. There is an increased supracardiac dulness and distinct bulge in the region of the pulmonary artery and left auricle. Such an appearance may be produced by a thymus.

September 9, 1920: *x*-Ray treatments to destroy the thymus commenced by Dr. G. W. Holmes.

Treatment was given with an interruptless type of machine using an 8-inch spark-gap between points, 4 mm. aluminum filter and one thickness of sole leather at a target skin distance of 8 inches in all except the last two, which were given at a distance of 10 inches.

Patient was given four treatments at three-week intervals. There was then an intermission of two months, when three more treatments at three-week intervals were given. All exposures were made over the thymus region, only one area used. About half the erythema dose was given at each sitting. There was no local or general reaction.

October 20, 1920: Still has some difficulty in swallowing, but feels much better.

November 1, 1920: Appears to have more facial expression, no ptosis.

September 23, 1921: Patient apparently in normal condition, works regularly eight hours a day, six days a week. Normal electric reactions in muscles of face and hands.

June 19, 1923: Patient is well and working regularly as a saleswoman.

**Physical Examination.**—*Pupils* equal, react to light and distance. No extra-ocular palsies, no nystagmus. No facial asymmetry or weakness. *Palate* moves freely. *Tongue* moves well in all directions, no atrophy. *Heart, lungs, abdomen:* Negative.

*Reflexes*—Elbow-jerks present and equal. Wrist-jerks present and equal. Abdominals present. Knee-jerks and ankle-jerks present and equal. Plantars normal. No ankle or patellar clonus.

Pain and temperature sense intact over legs and arms; distinguishes readily between sharp and blunt over arms and legs. Disks and vessels of fundi are normal. Electric reactions are normal in facial and hand muscles.

#### SUMMARY

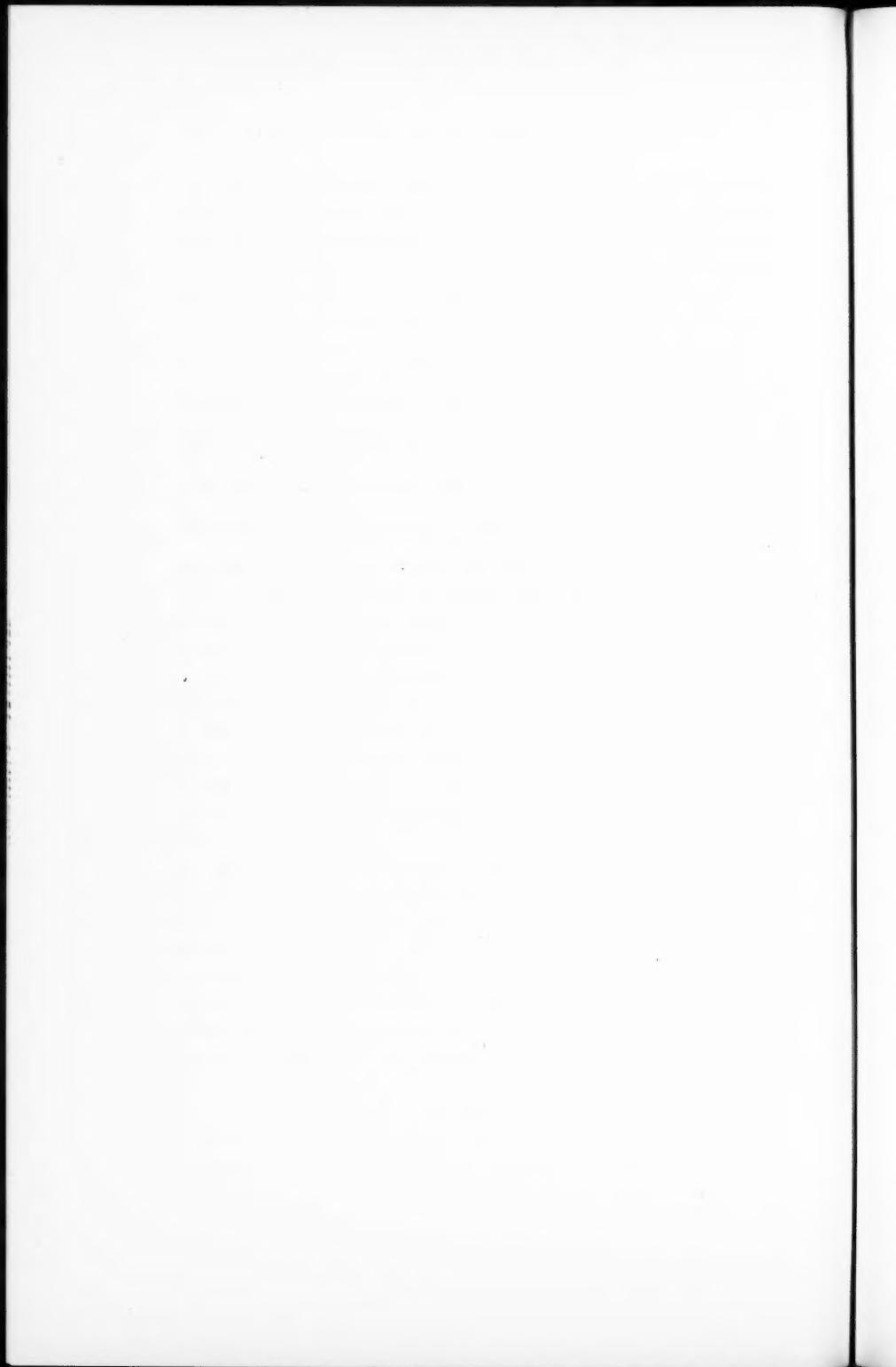
From a review of the literature and these 2 cases it seems logical to conclude that there are cases of myasthenia gravis in

which abnormalities of the thymus may be found. It also suggests that this is a syndrome and not a disease entity, as cases have been reported in which no abnormality of the thymus was discovered.

The myasthenic syndrome may follow on tumor of the thymus and disappear on irradiation of the thymus region.

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## CLINIC OF DR. HENRY JACKSON, JR.

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### A CASE OF RUPTURED ANEURYSM

THE case I wish to present today is a most unusual one:

J. D., fifty-one years old, a worker in a woolen mill, entered the hospital Christmas day, 1922. Two nights previously the patient and his entire family had eaten heavily of some "home baked" beans bought at a nearby delicatessen store. So far as could be ascertained they ate nothing else of consequence at that meal. About an hour afterward all 3 (husband, wife, and son) were seized with violent vomiting, severe diarrhea, spasmodic cramps in the arms and legs, and an intense craving for water. There was no chill. So great was the prostration that they were unable even to call a doctor or let anyone know of their illness. Two days passed. The husband was then able to crawl downstairs for help. The local physician advised the entire family to go to the hospital. The husband was admitted to the Fourth Medical Service. The wife and son did not come under the writer's observation.

On entrance the patient was still vomiting, though less frequently and less violently than during the preceding two days. The diarrhea had virtually ceased. He complained of slight cramps in the arms and legs, his thirst was still excessive, but he was now able to keep water down.

The family history was negative, save for the fact that one brother had died at twenty-one of pulmonary tuberculosis, and there was evidence of more or less intimate contact between this brother and the patient.

He had been married four years and had no children of his own. There was one stepson. His wife had had no miscarriages. His habits were good. Tea and coffee in moderation. No alcohol or tobacco used. He had been for the last twenty-five years a weaver in a woolen mill, working eight or nine hours a day and exposed to a dry and dusty atmosphere.

His past history again was negative except for the important fact that he had syphilis eighteen years ago. For this at the time of infection he had no treatment, but latterly he had had fairly vigorous treatment with salvarsan; no iodids or mercury were given so far as could be ascertained. There were no symptoms pointing to circulatory diseases, or disturbances of the lungs, gastro-intestinal or genito-urinary tracts. The memory was good and there have been no symptoms of nervous disorders.

On entrance the physical examination disclosed a well-developed and well-nourished man of middle age, obviously very ill. He complained of cramps in the arms and legs and a dull pain in the chest, relieved somewhat by sitting up. He was mentally clear and co-operative. The face was drawn, anxious, and considerably flushed. The skin was moist and smooth. The pupils were regular and reacted normally; the scleræ showed no jaundice. There was no rash. The throat was negative. His respirations were normal, 22 a minute. The chest was normal. The lungs were clear throughout and presented no abnormalities of any kind on careful examination.

The pulse was rapid—100 to 105. There was no peripheral arteriosclerosis. The heart was normal in size, the sounds of good quality. No murmurs or thrills could be made out. The supraventricular dulness was not increased, nor were there any abnormal pulsations in the region of the great vessels. The blood-pressure was 130/80.

The abdomen was negative. The spleen could not be felt. There was no abnormality of sensation and the reflexes were normal or slightly hyperactive. His temperature was normal. The patient's urine on entrance was acid, showed no albumin, and had a specific gravity of 1025. In the sediment were found

a few hyaline and granular casts and about 5 or 10 red blood-cells per high-power field. These abnormalities cleared up gradually and were almost gone at the end of ten days. The Wassermann was positive. The white count 8500.

His wife and son presented a very similar picture; they both continued to improve and were well in a week or ten days.

The patient's condition improved steadily for three days, and then, on December 28th, five days after his initial illness, his temperature rose to 99.5° F., the pulse jumped to 120, and the respirations showed a tendency to be more rapid. He seemed nervous and apprehensive, but made no complaints. The physical examination remained essentially negative.

On January 1st, nine days after the onset of symptoms (his wife and son were virtually well by this time), he began to complain of pain and constriction in his chest, similar, he said, to an attack which he had six years previously, and which was "cured" by salvarsan. His temperature rose to 101° F., his pulse remained rapid, but of good quality. On January 4th, while being examined by a student, he suddenly said, "Get out of here, I'm sick." There was excruciating precordial pain and he fell back on the pillows. The face became ashen gray. The pulse disappeared from the wrist, and the patient said he had an urgent desire to move his bowels, but he was unable to do so. He sweat profusely. The respirations rose to 44 a minute. Thirst was excessive. There was no vomiting. Within half an hour the pain had virtually ceased, but the patient looked and acted like a man in profound shock.

The lungs presented no abnormalities whatever. The heart sounds were weak and the pulse rapid and thready, but there was no increased cardiac dulness and no murmurs could be heard. There was no tenderness in the abdomen. Blood-culture was negative.

The next day, January 5th, examination showed the heart pushed to the right to such an extent that the right border of dulness was 2 cm. to the right of the sternum. The heart sounds were best heard in the midsternal region. Over the left lung area both in front and in back the percussion note was dull

and there was distant bronchial breathing. Tactile fremitus over this area was, if anything, decreased. There were a few scattered râles.

On January 7th the left upper back was tympanitic and over this area there was distant amphoric breathing. The heart was pushed still further to the right. A chest tap was done and 75 c.c. of unclotted blood was withdrawn. A culture of this fluid showed *Bacillus paratyphosus B*. The organism gave all the characteristic sugar reactions and was agglutinated by immune sera in dilutions up to 1 : 800.

During the next four days the patient grew more and more cyanotic, the temperature varied between 100° and 102° F., the respirations were 40 to 60, and the pulse about 130. He vomited occasionally. The left chest was perfectly immobile, flat at the base, with absent tactile fremitus, tympanitic above the angle of the scapula, with very distant amphoric breathing, or at other times no breath sounds at all. There was no hemoptysis, no hematemesis, no cough. He complained of no pain, but lay in a state of semistupor, very apprehensive when aroused.

January 10th, eighteen days after the onset of symptoms, and nine days after his precordial pain and collapse, the respirations rose to over 60 a minute, and he died.

Now the first point of interest is obviously the initial gastrointestinal upset which prostrated the entire family on December 23d. Food poisoning it certainly was. But what was its source and nature? Of course, the data obtained are, from an epidemiologic point of view, inadequate, but the possibilities may, nevertheless, be considered.

It should be noted that the onset of symptoms as early as one hour after eating the pork and beans would tend, if anything, to exonerate this food from having anything to do with the attack. Poisoning due to chemical decomposition products —the ancient ptomain poisoning—is certainly of great rarity and probably does not exist; and there is no evidence in this case that any ordinary chemical poison, such as arsenic or oxalic acid, had gotten into the food. Such a possibility was not, however, definitely ruled out, and it is not uncommon for

some household chemical or disinfectant to get into the food and give rise to symptoms erroneously attributed to food infection or intoxication. If the infection was indeed due to the pork and beans, it certainly constitutes a remarkably short incubation period, and it would seem that some preformed poison must have been present in the food, though the nature of the poison must remain a matter of speculation. In this connection it is interesting to note that some of the very shortest "incubation periods" reported have been in cases of mussel poisoning, in which fatalities are said to have occurred two hours after ingestion, and while the effects in this type of case were formerly thought to be due to "ptomaines," there is a growing belief that they are, in reality, due to "the *Bacillus enteritidis* of Gärtnér or one of its congeners" (Dr. M. J. Rosenow, Nelson Loose Leaf Medicine, vol. 2 p. 625). It is perfectly certain, however, that the infection was initiated at the evening meal which was so closely followed by the symptoms; for the husband, who had been away for months, had just that afternoon returned, and the only meal eaten by all three members of the family together was that immediately preceding the attack.

The beans, pork, and molasses from the store were examined bacteriologically and found negative. Moreover, no other food infections were reported from the vicinity, though the same lot of beans and pork was said to have been sold to scores of other people. Yet in the instance under consideration nothing was added to the beans before serving (cream, catsup, etc.), and from a sample remaining in the house *Bacillus coli communis* was cultivated and identified by its sugar reactions. Unfortunately no agglutination tests were done, so that paratyphoid B might have been present along with *Bacillus coli communis* and still have been missed, as can readily be seen from a consideration of the sugar reactions of the two groups. Paratyphoid B was positively identified in the blood of the pleural cavity of the patient, and the clinical course of the latter was by no means inconsistent with paratyphoid food infection. The early lack of fever is not against the diagnosis in the face of such extreme prostration. Much the same picture was seen in Russia

during the recent cholera epidemics. The cramp-like pains in the arms and legs were probably due to the excessive fluid loss from vomiting and diarrhea, though in this particular case the associated chest pains may very well have been due to syphilitic disease of the aorta. The blood and casts in the urine cannot be adequately explained on the basis of food poisoning, and we are left more or less in the dark as to the causative factor of these findings, unless, as is not unlikely, they were due to an exacerbation of a chronic nephritis.

With full realization that all the evidence is not in and that the data obtained are far from convincing, we may conclude that the presence of *Bacillus coli communis* in the pork and beans and the identification of paratyphoid B in the pleural fluid, together with a clinical picture not inconsistent with paratyphoid food infection, makes this diagnosis probable. For paratyphoid may well have been present in the beans and yet have been missed in the absence of agglutination tests. Indeed, without this somewhat weak hypothesis it is difficult to account for the simultaneous prostration of the whole family and the paratyphoid organisms in the patient's bloody pleural fluid. But even with these assumptions no ultimate source of the organism could be found, and the possibility still remains that all the symptoms were due to the presence in the food of some ordinary chemical poison and that the bacteriologic findings were not of etiologic importance. The case illustrates the difficulty of thoroughly clearing all the evidence relating to the problem, especially when the patient is admitted to a large general medical service where complete investigation is virtually impossible in every case.

On January 4th the sudden excruciating pain substernally, the collapse, the sweating, the rapid pulse, and the sense of impending dissolution indicate strongly some sudden and violent mechanical disturbance, such as rupture of the lung, a coronary embolus, or the rupture of an aneurysm; the tearing of the intima of the aorta is associated with just such a pain as this, and the symptoms may temporarily subside before the inevitable lethal outcome. Coronary embolus to give such in-

tense symptoms would necessarily be of wide extent, and instant death would probably have followed. There was no evidence of previous lung disease, no emphysema, no tuberculosis, no signs or symptoms of lung abscess. The possibility of an aneurysm should always be borne in mind in syphilitics who present obscure chest signs, and the advent of such a train of violent symptoms as these might well be due to the rupture of an aneurysm. Boiret reports 195 ruptures in 349 cases, and the commonest sites of rupture in his series were esophagus, 40, left pleura, 36, pericardium, 29. Other series vary in the distribution, but all agree that the left pleural sac is a common site for rupture. Death is frequently immediate, but may be delayed for days, and, indeed, cases have been reported where temporary recovery has followed even a fairly large hemorrhage.

The next morning there appeared signs of fluid in the chest: flatness, decreased tactile fremitus, increased sense of resistance, and immobility on respiration. The development of tympany above this fluid with distant amphoric breathing and marked displacement of the heart to the opposite side made the diagnosis of hemopneumothorax probable, and the withdrawal of blood from the pleural cavity clinched the diagnosis.

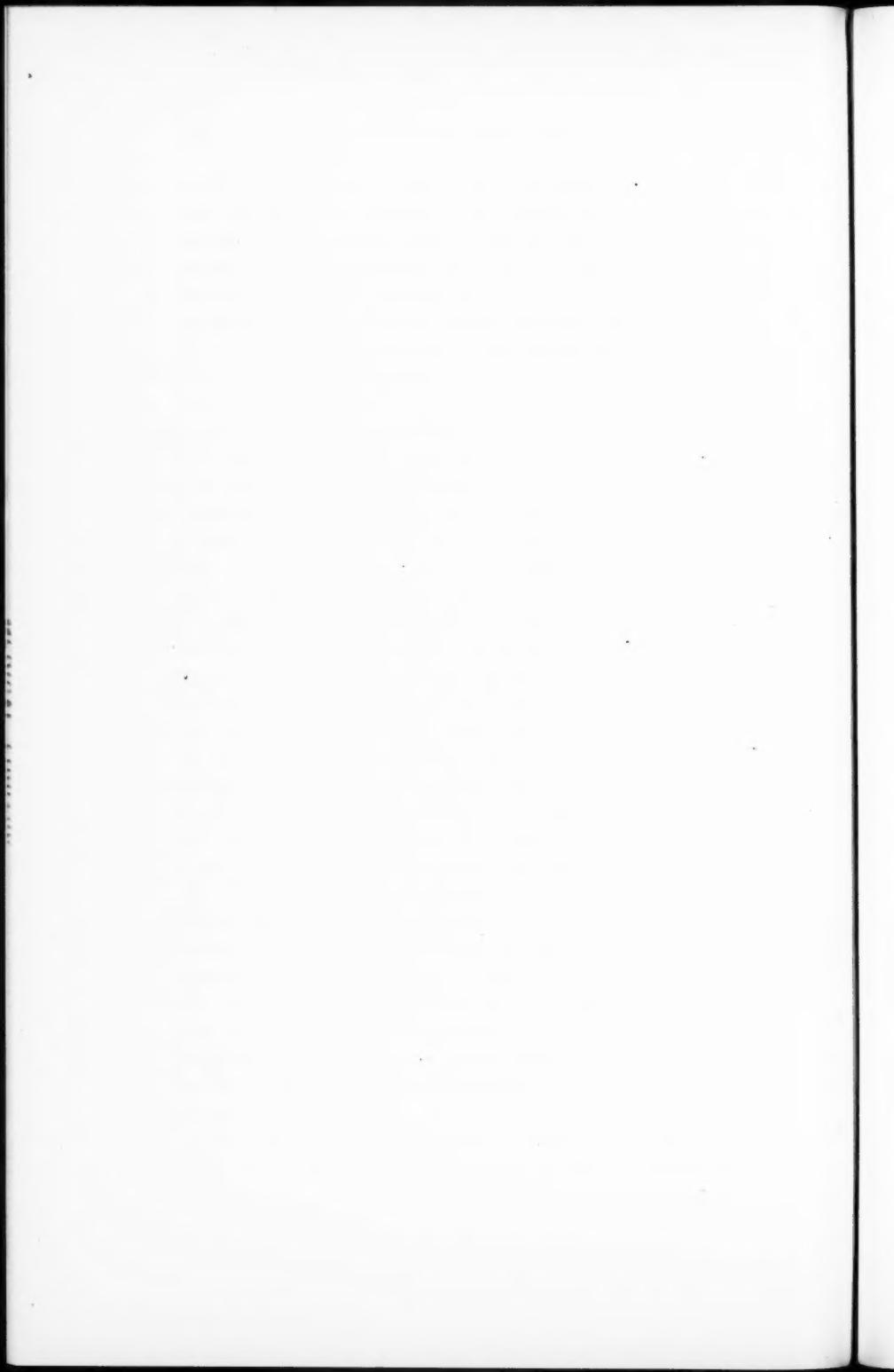
Now pneumothorax is, of course, due, in the vast majority of cases, to tuberculosis, and we have no signs or symptoms of that disease in this patient. It may, however, be due to the rupture of an emphysematous bleb in the lung, rupture of a carcinoma of the stomach, intestines, or esophagus into the pleura or the opening of a lung abscess. Of 18 proved cases of pneumothorax coming to autopsy at the Boston City Hospital, 15 were due to tuberculosis, 2 to rupture of a lung abscess, and 1 to an undetermined cause. Levy, Finley, May and Gebbard, and Hamilton have all reported pneumothorax due to the growth of various gas-producing organisms in pleural exudate. Hemothorax, on the other hand, may be due to rupture of an aneurysm, erosion of thoracic vessels by disease, penetrating wounds, or again, to tuberculosis. The one case of hemopneumothorax coming to autopsy at the Boston City Hospital (5000 autopsies) was due to tuberculosis.

We have then, in this case, a syphilitic, it should be remembered, sudden collapse with terrific substernal pain, followed in a day or so by the development of a pneumohemothorax. The diagnosis of rupture of an aneurysm of the aorta into the left pleural cavity was made, and the pneumothorax was explained as being due either to the tearing of the lung by the rupture or the growth of a gas-producing organism in the blood. The food poisoning was thought to be a precipitating factor in the rupture.

An autopsy was performed by Medical Examiner, Dr. Timothy J. Leary. The following is a condensation of his report which he was kind enough to put at the writer's disposal: There is an escape of gas on opening the left pleural cavity. The latter contains 2850 c.c. of largely fluid blood. The left lung is completely collapsed. The kidneys show chronic nephritis. At the junction of the descending arch of the aorta and thoracic portion there are adhesions over the left lateral surfaces of the bodies of the fifth and sixth dorsal vertebræ, separations of these adhesions resulting in the exposure of a cavity 5 by 6 cm. in the bodies of the sixth and seventh dorsal vertebræ. On opening the aorta there is found in this region an oval opening which terminates sharply with thick edges fitting the edge of the cavity in the vertebræ. The opening in the aorta is accurately filled with a firm, stratified clot. In the midthoracic aorta there is a tear almost at right angles 5 cm. in width and undermining the wall for a distance of 2 cm. The aorta showed a few small areas of sclerosis. The left lung is collapsed and its surface covered by a layer of rather intimately attached clot. Behind the apex there occur adhesions over the region occupied by the aneurysm. Here in dissecting out the aneurysm there were made incisions into the lungs, but the pleural surface is smooth and intact except for these artefacts. The rest of the autopsy showed nothing of interest to the present discussion. There was no ulceration in the intestines.

The postmortem examination confirms the clinical diagnosis. The right angle tear in the aorta was, in all probability,

the cause of the terrific substernal pain. The hemothorax was a consequence of the rupture of the opening in the aorta. The pneumothorax was not, as far as could be determined, due to any tear in the lung. It may have been due to the growth in the bloody fluid of some gas-producing organism. The relation of the food infection to the rupture of the aneurysm is problematic, but it was no doubt a precipitating factor.



## CLINIC OF DR. FRANK B. BERRY

FROM THE MEDICAL SERVICE OF THE BOSTON CITY HOSPITAL,  
CLINIC OF DR. F. W. PEABODY

### MYOCARDITIS IN YOUTH

IN the consideration of myocardial involvement in infectious diseases diphtheria and the rheumatic infections—acute articular rheumatism, tonsillitis, chorea, myositis—immediately come into one's mind, and of these, the latter group is by far the more important. In Pratt's opinion "rheumatic fever injures the heart of almost every child it attacks," and adults, although more immune than children, nevertheless suffer from this complication all too frequently. It is now pretty generally recognized that the endocardium and the pericardium are rarely attacked alone, but are almost always accompanied by myocardial participation. Myocarditis, on the other hand, often occurs by itself, so far as can be determined, and many instances of hitherto unsuspected acute lesions are now being brought to light.

This improvement in diagnosis may be ascribed to two factors: (1) increasingly careful observation combined with a better understanding of the finer anatomy and physiology of the heart; and (2) the development and use of the polygraph and electrocardiograph. For, without question, many examples of temporary acute myocarditis occurring in the course of acute rheumatism or tonsillitis can be recognized only with the aid of one of these instruments. Indeed, a rheumatic condition may first manifest itself as a carditis. Fulton, in an unpublished article, has reviewed a series of such cases reported by several writers and, in addition, describes a similar one of his own, where the initial symptoms of infection were those of a partial

acute heart-block, the diagnosis of which was definitely established only by the electrocardiogram.

Up to about fifty years ago but little attention was given to the possibility of myocardial involvement except as a sequel to diphtheria, and possibly also to typhoid fever and pneumonia. With the rheumatic group all the stress was placed upon the endocardium and pericardium. Since then, however, the myocardium has been considered more and more as the site of an acute process—*toxic* or *true inflammatory*—during a rheumatic infection. Until 1905 this recognition was largely clinical except in so far as hypertrophy, dilatation, and old myocardial scars were noted by the pathologist.

In that year Aschoff and Tawara, while studying a number of hypertrophied hearts to find out, if possible, why they were less efficient than normal, came upon certain collections of cells in some of them. These were submiliary nodules of endothelial cells and fibroblasts with a small amount of fibrin, and were always perivascular or else marked the location of a former capillary.

Since then Coombs has studied these further, and has shown that they always arise from capillary endothelium. He found that they were constantly present in active phases of cardiac rheumatism and constantly absent in the later cicatricial stages. "The final stages of postrheumatic disease of the heart are free from these phenomena, and the patient dies of degenerative changes in the myocardium largely, if not wholly, initiated, sustained, and completed by the mechanical embarrassments which these cicatricial changes impose on the action of the heart." In addition, he described very similar nodules occurring in one case of scarlatinal carditis and one of subacute bacterial endocarditis. He also states that in the ordinary streptococcus infections the lesions in the heart are more marked. They are embolic in character, diffuse, and show foci of organisms, poly-nuclears, small infarcts, and irregular collections of endothelial cells from the vascular endothelium. In a number of rabbits inoculated with streptococci obtained from various sources inconstant cardiac lesions resulted. These consisted of cocci,

polynuclears, fibrin, and endothelial cells; the last named formed the most striking element of the reaction. Coombs concludes, therefore, from his very extensive study that all of the above described lesions are sufficiently similar to show a probable relationship; hence we may say that although typical Aschoff nodes have been found in the heart only in active rheumatic infection, yet very similar lesions may also be found in certain other conditions.

The same author in an earlier publication divided the cases of heart complications following rheumatism into four groups: 1, This, the largest and most important, includes those cases in which there is some general cardiac enlargement associated with the signs of mitral insufficiency. 2, Those showing the same plus a pericarditis. 3, Those in which there is definite evidence of an additional valve lesion. 4, A rare group of malignant endocarditis. Two of the cases in the first group died, and at autopsy showed merely enlarged and dilated hearts. A similar picture is occasionally seen in the postmortem room of any large hospital. These, therefore, are purely myocardial deaths, and this is most often the cause of death in children and adolescents who die from heart failure following rheumatism.

But now what takes place in the less severe types of myocardial involvement? Much, of course, depends upon the lesion itself. Should it be located in the conducting system, we should expect some disturbance of the conduction time, with perhaps the development of a varying degree of true acute heart-block. This is exactly what happens, as may be clearly demonstrated by the polygraph or the electrocardiograph. Depending upon the extent and severity of the lesion the P-R time in the electrocardiogram may be increased or there may even be an actual blocking of auricular impulses, which, again, may be only temporary, may persist for some time, or may be permanent, according to the character, extent, and persistence of the inflammatory reaction.

Should this region escape and other portions of the musculature be involved, the clinical picture may vary greatly. There may be simply instability and rapidity of rate, with or without

evidence of slight enlargement or the appearance of a soft systolic murmur. As Hutchison says, the signs may be very indefinite, with a practically normal temperature and the pulse-rate and stability of the pulse as the best guide. Again, ectopic beats may appear and may be associated with a heart-block. If the process becomes more marked and extensive, there may ensue a gallop rhythm and actual cardiac failure with lowered vital capacity and other signs of decompensation. Auricular flutter or fibrillation may rarely occur, though these are more likely to appear later rather than in the acute stages. Laubry and Donner, however, have recently reported an example of auricular fibrillation coming on in the midst of an initial attack of rheumatic fever in a man of thirty-three. Furthermore, after the paroxysm had been stopped by quinidin it was interesting to note that the P-R time was very much increased. Sometimes, indeed, no changes at all may be apparent clinically, and it is only by the aid of the electrocardiograph that such may be detected. It is for this reason that every case of rheumatic or diphtheric infection should be followed with electrocardiographic study as well as clinically, for otherwise slight lesions are bound to pass unnoticed at a time when further damage might be most easily prevented.

During the past year three such examples of myocarditis in young people have come to the attention of the writer. The first two have been studied under Drs. Peabody and Mallory at the Boston City Hospital, and the last one has been seen in conjunction with Dr. J. H. Pratt. The first of these cases is of particular interest in that it is one of pure rheumatic myocarditis without any valvular involvement, and very probably no pericardial involvement, although a small milk patch was found upon the pericardium at autopsy.

It is seldom that the myocardium, when once the site of such an extensive process as is present in Case I, goes on to apparent temporary complete recovery and to death a few years later from heart failure without either further reinfection or valvular disease. Although we have no absolute proof that the myocarditis in this instance was rheumatic in origin, yet

the presumptive evidence in favor of this is very strong in view of the history, the absence of any other probable etiology, and the findings at autopsy, which correspond exactly with the very late or healed stages of rheumatic myocarditis as pointed out by Coombs.

#### CASE I

Rheumatic fever; myocarditis; death eight years later.

A. McN., age twenty-nine, a clerk.

**Family history negative.**

**Past History.**—Pneumonia twice in early childhood. Typhoid fever at nineteen, followed by phlebitis. Rheumatic fever eight years ago, with complete recovery. Influenza two years ago. Sore throats one or two every winter.

**Present Illness.**—Perfectly well until two and a half months ago, when he had a cold and cough associated with some sore throat. He did not go to bed, but stayed at home two days. Then he returned to work for a week, when he noticed marked dyspnea on moving about. This was relieved by rest and digitalis at home. For three weeks before admission he has had a mild cough with a small amount of white sputum. This cough precipitated mild precordial distress, which lasted about half an hour. Admitted May 11, 1922.

**Physical Examination.**—Negative except as to the heart. The apex impulse was diffuse and heaving and felt best in the sixth space. The right border was  $4\frac{1}{2}$  cm. from the midline and the left 14 cm. The rate was 80. At the apex and transmitted to the left was a soft blowing systolic murmur. Extrasystoles appeared at every fifth or sixth beat. There was marked dyspnea and the patient had an anxious expression. The lungs were clear and there was no edema or liver tenderness.

Blood Wassermann and urine were negative. The x-ray showed the heart to be enlarged in all directions. An electrocardiogram taken June 9th showed an intraventricular block and many ectopic beats.

He left the hospital on July 29th, and caught cold the day following, which resulted in a bad cough and considerable dyspnea. At that time he began to have attacks of nocturnal

dyspnea, and these increased. He grew progressively worse and weaker, and entered the hospital again August 10th.

**Physical Examination.**—Moderate dyspnea. No cyanosis or edema. Musical râles throughout both chests. The heart was as before, except that now there was a gallop rhythm.

Electrocardiogram taken September 9th showed intraventricular block, right bundle branch. Partial A-V block with a P-R time of 0.24 second. Rate 83. Auricular hypertrophy.

The blood-pressure persisted at about 90 to 100 systolic, and 60 diastolic. The pulse varied between 50 and 110. On October 16th his respirations went from 25 to 30, and on the 19th to 35, and signs of consolidation appeared in his left back. The temperature was 102° F. rectal. The sputum showed pneumococcus Type 1. The white blood-count was 19,600 as against 8400 on admission. Patient died October 22d, within eight months of the onset of his first cardiac symptom and following a steadily progressive cardiac failure.

The day following his death, Dr. Peabody dictated the following note: "This patient came into the hospital about six months ago with cardiac decompensation of rather recent development. In spite of a definite history of acute arthritis, which was apparently rheumatic fever, the physical examination gave no evidence of valvular disease. It is apparently pure muscular insufficiency such as occurs very commonly in older persons, but a finding that is remarkable in a person as young as the patient. The clinical diagnosis of myocarditis was confirmed by the electrocardiogram, which was interpreted as indicating a block in the right branch of the conducting system. This leads us to suppose that other and more diffuse areas of fibrosis were also present. With prolonged rest and digitalis he made some improvement, but never gained as rapidly as was wished. He was finally discharged because he did not seem to be improving further and desired to go home. After a short time he returned to the hospital again in this, his present, admission. He had done little while outside, but again became decompensated. The history of progression in symptoms without due cause made the prognosis bad. On

this admission he has never done well, and although he was comfortable for some time, he began to develop dyspnea even while at rest in bed some weeks ago. He has had rather constant digitalis therapy, but has never made more than slight temporary improvement. The physical signs in the heart have changed very little during these weeks, and no definite murmurs, except a soft systolic at the apex, have been audible. The only physical sign of importance has been a gallop rhythm at the apex protodiastolic in type. This has remained constant and has become extraordinarily marked, so that it could be easily demonstrated to the students. The gallop rhythm was associated with an easily visible double impulse at the apex. A few days before death he became worse. The dyspnea was more marked. Two days before he died I saw him, and found him extremely weak and pale, with a little cyanosis of the lips and finger-tips. The pulse was weak and variable in force. The blood-pressure was very low and the pulse was easily obliterated. The question was discussed as to whether he had a cardiac infarct, but he had complained of no pain. (It is interesting that some hours before death he complained of pain in the upper abdominal region.) Both lungs were full of coarse râles in front and back, and it seems quite possible that this condition might be largely due to pulmonary infection. His temperature was normal by mouth, but it seemed that this might be inaccurate owing to his dyspnea, and a rectal temperature was taken and he was found to have fever. The leukocyte count was high, and a diagnosis of bronchopneumonia was made. He gradually became worse and responded to no treatment. Death was apparently due to a chronic myocarditis with a subsequent development of bronchopneumonia."

At autopsy, October 23, 1922, seven hours after death, numerous fresh fibrinous adhesions were found binding the right lung to the parietal pleura, and there were about 100 c.c. of clear fluid in the pericardial cavity. There were patches of bronchopneumonia throughout both lungs, together with bronchitis and congestion. Chronic passive congestion was present

in the liver and kidneys and there were soft yellow patches along the aorta.

Heart, weight 740 grams. "It is very large and rather soft. The surface shows many petechial hemorrhages. On the

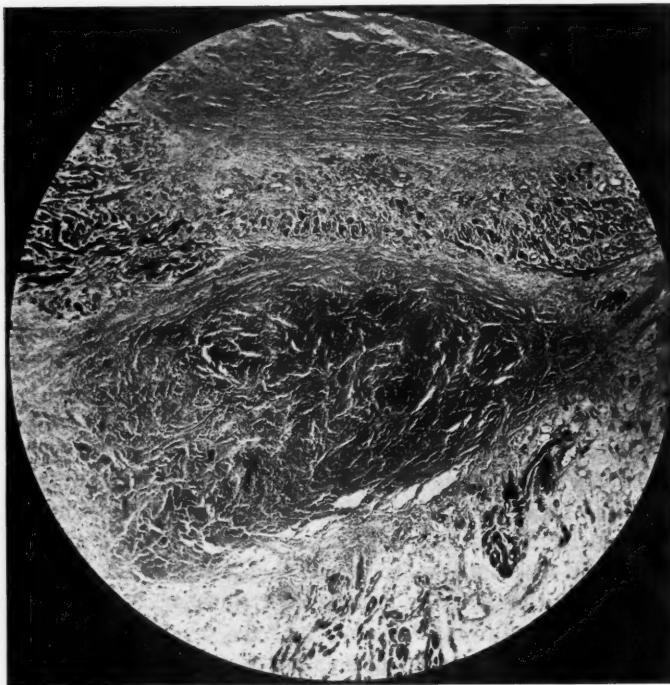


Fig. 156.—Section through the bundle of His, right auricle. The bundle is almost completely obliterated by scar tissue; the normal muscle-fibers of the bundle may be seen on either side. Large mass of scar tissue directly beneath.  $\times 100$ . (Photomicrographs by Dr. J. B. Mallory.)

surface of the right auricle is a radiating thickened area of scar tissue. As the heart lies on the board it measures 20 cm. from the auricular appendages to the apex, the greatest width is 16.5 cm., the height 7.5 cm. It is especially dilated at the apex, which is round instead of conforming to the usual shape.

The muscle is reddish brown and thin. The chordæ tendineæ and papillary muscles appear normal, but on section the latter are in large part replaced by fibrous tissue, and areas of fibrosis are found throughout the wall of the left ventricle. No valve lesions are found, but the entire endocardium of the left heart

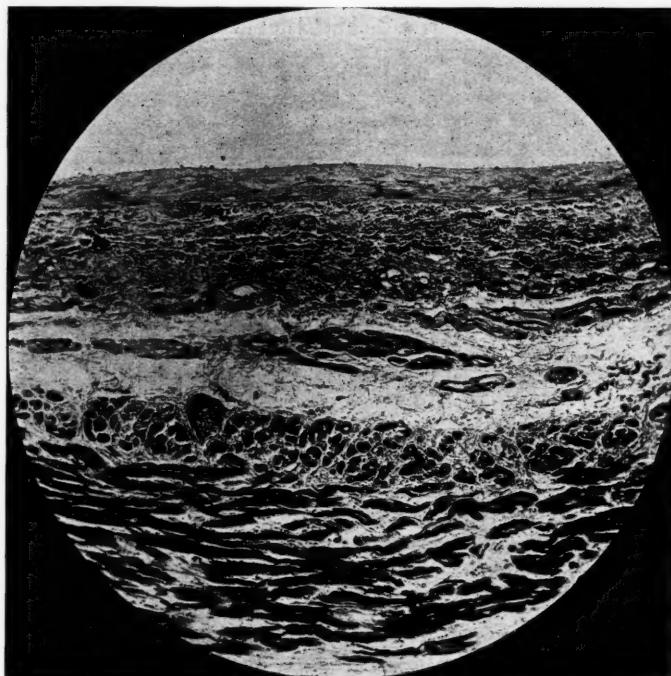


Fig. 157.—Section through the interventricular septum. Endocardial surface and layer of Purkinje cells and scar tissue.  $\times 100$ . (Photomicrographs by Dr. J. B. Mallory.)

is thickened and yellowish gray. At the apex is a dark red pyriform swelling, soft in the center, attached to the endocardium. Numerous smaller thrombi are found scattered about the indentations of the wall. A few strands of thickened tissue are found just below the pulmonary valve. The coronary

arteries are not remarkable. Measurements: Tricuspid valve, 16 cm.; pulmonary valve, 8.5 cm.; mitral valve, 14.5 cm.; aortic valve, 8.5 cm.; thickness of left ventricle, 0.6 to 1.2 cm.; of right ventricle, 0.5 cm."

**Anatomic Diagnoses.**—Hypertrophy and dilatation of the heart; diffuse healed endocarditis; fibrous myocarditis; thrombi



Fig. 158.—Papillary muscles of left ventricle largely replaced by scar tissue.  
× 100. (Photomicrographs by Dr. J. B. Mallory.)

of ventricular wall; bronchopneumonia; acute fibrinous pleuritis; healed perihepatitis, perisplenitis, pleuritis, and pericarditis; chronic passive congestion of the liver and kidneys.

**Histologic Examination of the Heart.**—Sections were studied from all portions of the heart. Scharlach R, hematoxylin-eosin,

eosin-methylene-blue, and Mallory's connective-tissue stains were used. Small fat-droplets are present in some of the muscle-fibers—a true fatty degeneration. The process is an old one, and everywhere there are large and small areas of fibrous tissue; this is most marked in the papillary muscles of the left ventricle, where in places only comparatively few strands of normal muscle remain. In some areas, for the most part small, there is a mild cellular reaction, chiefly lymphocytes, but occasionally a few polymorphonuclears also. This extensive scarring extends up to and involves many of the Purkinje fibers. In a section through the node of Tawara and main stem of the bundle fibrous tissue and lymphocytes are seen almost transecting it at one point. The endothelium of the left auricle and ventricle is uniformly thickened and appears much as it would if composed of layers of hyalinized fibrin. The vessels are, for the most part, negative, but some of those in the scarred areas have some endothelial thickening. No Aschoff nodes were found, but this is undoubtedly due to the fact that the process is in the late healed stage.

#### CASE II

Diphtheria; myocarditis; paralysis; recovery.

E. R., age twenty-nine, policeman.

**Family history** negative.

**Past History.**—Rheumatic fever six years ago. Tonsillitis two years ago. No history of chest pain, dyspnea, palpitation, cough, or hemoptysis. Lost 25 pounds in past month. Habits good. No venereal history, alcohol, or tobacco to excess.

**Present Illness.**—On December 8, 1922 he complained of a sore throat and was in bed two and a half weeks. There was a membrane on his throat, but one culture was negative for diphtheria. About Christmas time he began to regurgitate fluids through his nose and to have difficulty in swallowing. A second throat culture was negative. He was given no antitoxin. On January 2, 1923 he reported back for duty, but at that time had tingling of his hands, about the tip of his tongue, and of his lower lip. He then began to have dizzy spells; weakness, and

dyspnea on climbing stairs, all of which increased until his admission to the hospital January 12th.

Physical examination showed sluggish pupillary reactions and weakness of his hands and legs, with some sensory disturbances in them. The heart was only very slightly if any enlarged, but the sounds were weak and there was a gallop rhythm. The vital capacity was 3050 c.c. and there was a distinct palate paralysis. He was seen by Dr. Place, who called his condition a typical postdiphtheric paralysis.

January 12th: Electrocardiogram taken showed an inverted T wave in Leads I and II, with a marked upward convexity of the S-T period.

February 21st: Electrocardiogram was normal. His vital capacity had gradually increased to 3900 c.c.

February 26th: Dyspnea suddenly became marked, there was vomiting, free perspiration, the heart again showed a gallop rhythm, and the vital capacity dropped to 2250 c.c. It was noted that the movement of the diaphragm was poor and this was confirmed by x-ray. Dr. Place considered the present change to be due to phrenic nerve involvement. Within the next three days the vital capacity dropped to 1950 c.c. After this he began to improve in every way, so that by March 17th his palatal paralysis had disappeared, his grip was better, the heart action was strong and the rhythm normal, and his vital capacity had risen to 3500 c.c. Improvement continued, and on March 31st his vital capacity was 4525 c.c. and his paralysis was improving steadily.

On admission the pulse was 100; it varied between 70 and 100 up to about March 1st, and has since been from 80 to 90. The blood-pressure was 135 systolic and 90 diastolic on admission, and 110 systolic and 60 diastolic March 31st. An electrocardiogram taken February 28th, just after his sudden relapse, was normal, which further substantiated the diagnosis of phrenic nerve involvement as the cause for his relapse.

**CASE III**

Rheumatic fever attacks; endocarditis and myocarditis; death six years later from cardiac failure.

H. B., age thirty, farmer.

**Family history negative.**

**Past History.**—Occasional attacks of tonsillitis. Rheumatic fever in the spring of 1916; a rather severe attack. He was cared for by two excellent internists, and no cardiac involvement could be found at that time. As soon as he had recovered his tonsils were removed and he suffered an exacerbation of his rheumatism for a week. He made a good recovery and felt well until the latter part of 1918, when he had an exceedingly severe attack of rheumatic fever and a murmur, and slight cardiac enlargement were noted at that time. He recovered from this slowly and ran a slight temperature for several weeks. In June, 1919 one hand and wrist were swollen for a week, and he felt poorly for some weeks afterward. In July, 1919 he entered the Peter Bent Brigham Hospital for study. Up to this time there was no evidence of pain in the chest, dyspnea, palpitation, or cough. Examination showed a diffuse impulse all over the precordium, with the impulse felt best in the fifth space 12 cm. from the midsternal line. The left border dulness was 13 cm. from the midline, 3 cm. outside the nipple line. The first sound at the apex was followed by a loud blowing murmur. There was a loud second and a dull third sound, giving a protodiastolic gallop rhythm at the apex. There was a faint diastolic murmur in the third space to the left of the sternum. Blood-pressure 110 systolic, 54 diastolic. Laboratory findings negative. He remained in the hospital two days and his pulse varied from 82 to 95 and his temperature reached 99° F. both afternoons.

His activities were limited and he did fairly well for the next year and a half. The writer noticed, however, that even at that time moderate exertion made him somewhat short of breath. In 1921 his father noticed that he was slightly dyspneic when he talked, and in July of that year he had a very mild attack of rheumatism, which involved his fingers and ankles. In

October he consulted his local physician for swelling of his abdomen, and at that time some edema of the feet and ankles was first noted. He was short of breath then even when quiet, and talking increased the dyspnea. He was in bed for nineteen days at this time, and was then allowed up and resumed his usual work about his place. During the winter and spring of 1922 he seemed definitely better until the onset of the present illness, which appeared quite abruptly.

**Present Illness.**—On May 1, 1922 he again consulted his physician for swelling of the abdomen. There was no fever. The pulse was 80 at the wrist and irregular for the first time. Blood-pressure 110/50. In spite of his condition he kept up and about for a week and traveled a number of miles by automobile each day. Dyspnea increased, however, so that by May 8th he was obliged to go to bed. On May 15th the conjunctivæ became slightly yellow and the stools were light colored. His bowels were kept open with Pluto water every other day and he was given morphin, gr.  $\frac{1}{4}$ , every night. He spent part of the time in bed and part sitting in a chair. He was seen by Dr. J. H. Pratt and the writer for the first time on May 19th. At that time he said that he had a dry cough for several months and that he had been taking small amounts of digitalis steadily for the past week—about 10 minims a day. He had vomited for the first time that morning. The breathing was labored, but he did not complain particularly of actual shortness of breath.

**Physical Examination.**—“Patient is in a semirecumbent posture. He is thin and there is a slight icteric tinge to the conjunctivæ and skin. Respirations are 22, but they are labored and superficial. No definite cyanosis. There is a large jugular pulse on both sides of the neck. There is frequent coughing.

“*Lungs:* The lungs are clear and no râles are heard anywhere. *Heart:* There is a wide area of visible and palpable pulsation from the second interspace to midaxilla, and below to the epigastrium, where it joins an area of marked pulsation. The whole left chest moves with each heart beat, but the impulses are weak. The heart action is rapid and very irregular. A thrill

can be felt between the left manillary and anterior axillary lines, but owing to the rapidity of the heart this cannot be timed. Right border dulness 4.5 cm. from the midline, and left border dulness is just inside the midaxillary line in the sixth and seventh spaces. The upper border of dulness is in the second left interspace. The rate at the apex varies from 108 to 120 and at the wrist it is 76. Two loud murmurs are heard over the mitral and tricuspid areas and a systolic murmur can be heard in the aortic area; the second sound is scarcely audible here. The pulse is small. *Abdomen:* Moderate distention. There is a wide area of epigastric pulsation corresponding to the liver, which extends about 4 cm. below the right costal margin. No dulness in the flanks. The feet are cold and cyanosed. There is evidently some diffuse swelling of the legs, buttocks, and anterior abdominal wall, but no pitting on palpation. A polygraphic tracing confirmed the diagnosis of auricular fibrillation with a ventricular hepatic pulse."

**Treatment.**—Absolute rest in bed was ordered. A Karell diet was instituted, and he was given 1 gram of digitalis leaf.

The patient continued to grow worse, and on the following day voided only 150 c.c. of urine. The heart still continued very irregular, but the rate had dropped to 80 and there was no pulse deficit. The lungs were still clear. About 3 A. M., May 21st, coarse râles were heard over both lungs, the heart sounds became feeble, and the rate increased. His condition gradually failed and he died several hours later. About fifteen minutes before death the cardiac rhythm suddenly became normal, with a rate of 90. This persisted until within two or three minutes of death, when it stopped momentarily, and then resumed a slow fibrillation.

This case is somewhat similar to the first in many respects. Here, however, the cardiac damage was more extensive and there was the usual valvular involvement. There was no necropsy. The enlarged heart was first noted during his second severe attack of rheumatic fever, and six months later there was a very marked amount of hypertrophy. This and his subsequent course can be accounted for only by extensive myo-

cardial as well as valve damage, and so is really an example of pancarditis.

#### SUMMARY AND CONCLUSIONS

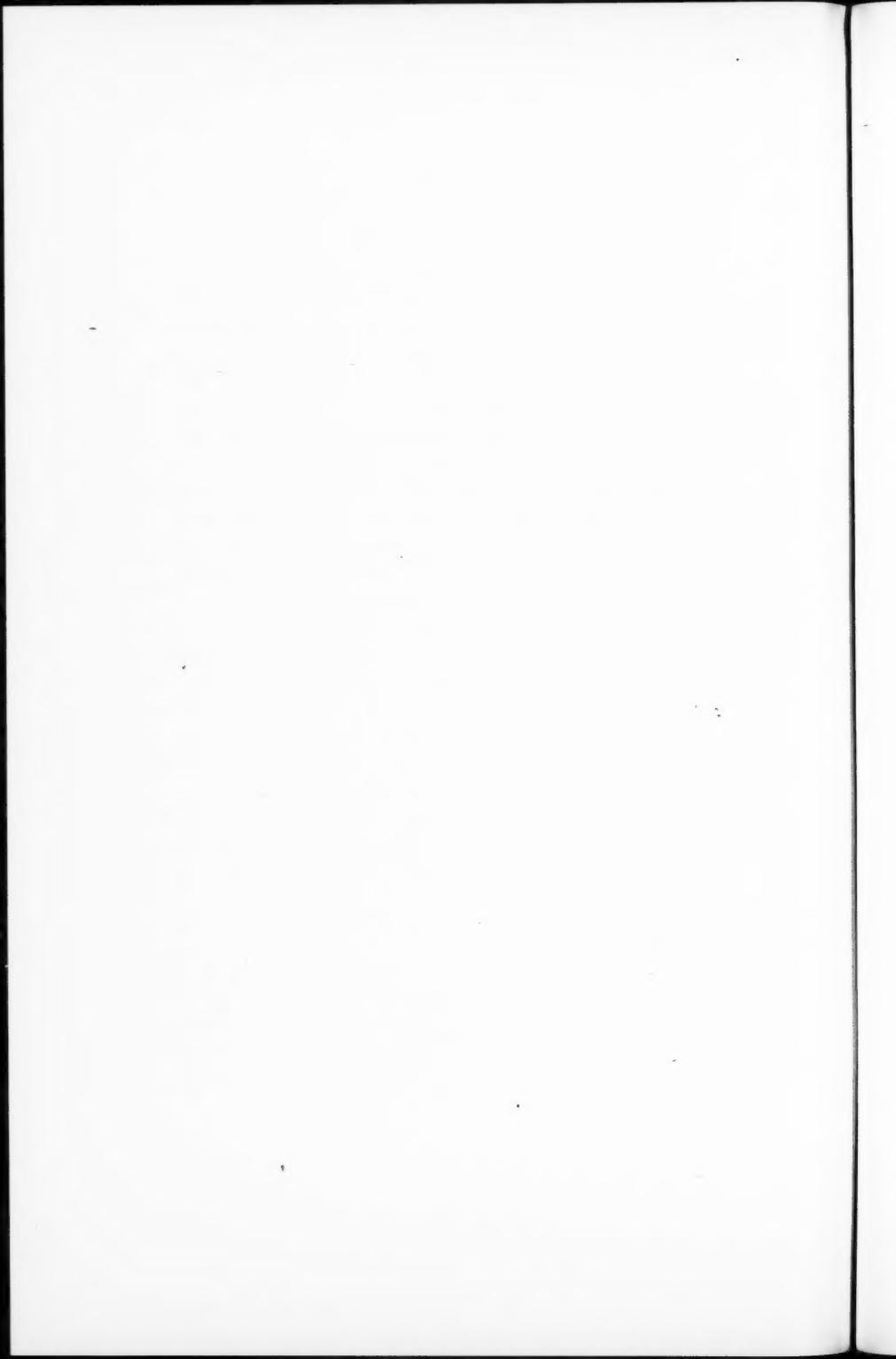
Three cases of myocarditis complicating rheumatism and diphtheria have been presented. The first and last are similar, although Case III pursued the more usual course. From a study of these and other like instances reported in the literature that has accumulated on this subject several conclusions seem warranted:

1. Acute myocarditis as a sequel to, or even initiating, infections of a rheumatic nature is a well recognized condition. It is usually associated with endocardial or pericardial involvement, or both. In the first case reported here, however, it occurred practically alone, and in its final stages the whole picture was almost identical with that commonly seen with the ordinary chronic myocarditis in older people.
2. In order to detect this complication in its early or mild stages extremely careful observation is necessary; sometimes, in fact, diagnosis can be made only by means of polygraph or electrocardiograph. It is therefore advisable, whenever possible, to take electrocardiograms on all patients suffering from the rheumatic group of infections or from diphtheria.
3. This condition should be constantly borne in mind in these infections, early recognition of it should be made, and adequate therapeutic measures at once instituted to prevent, if possible, any further damage to the myocardium.
4. In the absence of, or with improper or inadequate treatment, the prognosis is grave as to a good recovery and also even as to life itself.
5. In the great majority of cases dying from cardiac failure during or within a few years following rheumatic infection death is due to myocardial involvement with lesions sufficiently extensive to cause a primary myocardial insufficiency. In these cases valvular disease, if present at all, plays a minor part.

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CLINIC OF MARY E. TRAINOR, R. N., AND  
DR. BRONSON CROTHERS

CHILDREN'S HOSPITAL

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**THE NON-OPERATIVE TREATMENT OF OBSTETRIC  
PARALYSIS**

In a clinic last year one of us discussed the effect of breech extraction upon the central nervous system. Today we wish to consider a less severe, more generally recognized, and equally important obstetric subject from a neurologic point of view. In particular we hope to convince you that treatment of birth injuries of peripheral nerves should be started early and kept up late.

Obstetric paralysis of one arm or, more rarely, of both seems to us perfectly easy to explain on neurologic grounds. In certain cases it is quite obvious that the cervical cord is injured. The average case, however, is evidently due to a paralysis or weakening of the muscles supplied by the fifth and sixth cervical segments. A considerable amount of valid evidence is recorded which leaves no doubt in our minds that the injury is due to stretching, often to the point of frank rupture, of the roots arising in these segments as they join to form the upper primary cord of the brachial plexus.

The method by which this stretching takes place is clear. Perhaps the simplest demonstration is by means of a dissection. In this preparation the plexus and cord are exposed from the front. One of us will hold the shoulders while the other draws the head forcibly to one side—two things will happen. The cord is drawn to the side of the spinal canal. The upper cord of the plexus is put on the stretch. Further lateral traction against the fixed head will, of course, eventually rupture some-

thing. In certain cases the roots pull out of the cord. Fortunately, such an accident is relatively rare. If the baby survives an injury of this type a serious interference with cord function seems almost inevitable. The roots may give way near the cord, in which case the sympathetic fibers are likely to suffer. This sympathetic injury is, of course, most likely if the whole plexus or the lower roots give way. Ocular signs will naturally follow.

In most cases, however, the point of least resistance is the point of function of the fifth and sixth roots. The logical result

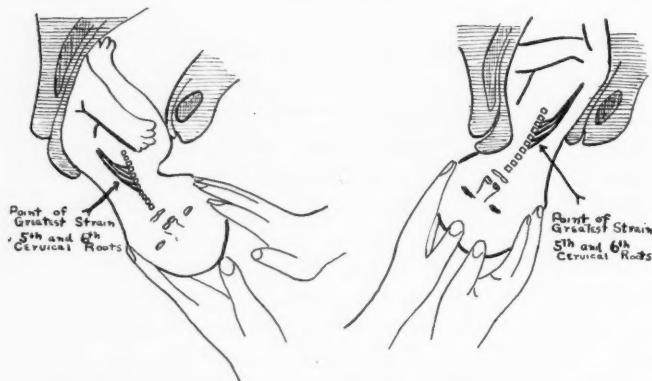


Fig. 159.—Diagrams illustrating stress upon plexus during conventional obstetric procedures in vertex delivery. On the left the posterior shoulder is caught; on the right, the anterior.

is weakness of the muscles supplied, without ocular signs or paraplegia.

That this mechanism can be brought into action in difficult or badly handled vertex deliveries is evident. I have made tracings from a standard obstetric text-book showing the procedure advised in normal vertex deliveries. Upon these I have sketched the spinal column and the plexus (Fig. 159). It is clear that duplication of these conventional procedures upon the dissection produced a considerable and perhaps unbearable strain. Of course, the more difficult the labor, the more likely

the injury. It is evident, too, that if the attendant pulls the shoulders away from the fixed head, in a breech extraction, exactly the same mechanism is brought into action. If time permitted it would be easy to show cases where both arms are partially disabled by undue use of obstetric force in extraction. However, in order to limit the discussion to a relatively simple problem we will confine our attention to the cases of the so-called "upper arm" type involving one arm.

**Case I.**—This baby, six months old, was delivered without any great difficulty, head first. After birth she did not move her right arm normally. She shows the typical "upper arm" type of paralysis (Fig. 160). The fingers move freely and there



Fig. 160.—Case I. Untreated early case.

is fair flexion at the wrist. The deformity is due to weakness of the deltoid, of the external rotators of the shoulder, of the biceps, and of the brachioradialis or supinator longus. The child, therefore, has difficulty in abducting and elevating the arm, in flexing the elbow, and in supinating the wrist. This is the typical disability we attribute to injury of the upper plexus.

This baby, at present, is crippled by weakness of certain muscles and by contractures of their antagonists. The question of prognosis is of vital importance. If complete recovery can be expected without treatment the condition is interesting, but not therapeutically important. Our only duty would be to establish the diagnosis by ruling out other possibilities, such as

fractures about the shoulder and injuries of the spinal cord. Apparently there is a very general impression supported by statements of experienced obstetricians that obstetric paralysis is a mild disturbance almost always ending in spontaneous recovery. To this conception we take vigorous exception. Dr. J. J. Thomas and Dr. J. W. Sever have reported from this clinic more cases than those recorded by all other observers put together. These babies come into this clinic at the rate of about 50 a year. Many of them have been under observation from the age of two weeks to the time they leave our care at twelve years. We believe that *complete* recovery, even with treatment, is exceptional. Therefore, we regard a passive policy based on a theory that all, or almost all, children with brachial palsy recover without treatment as indefensible.

On the other hand, it is clear that the arm may be fairly useful and the disability may be concealed. As you see, the fingers are relatively efficient. The most serious difficulties are due to inability to raise and to rotate the arm at the shoulder and to supinate at the elbow and wrist. Neither disability prevents a considerable use of the arm, and each can be and often is concealed throughout life. Even so, this relatively inconspicuous deformity limits normal activity and is not consistent with a proper conception of *complete* recovery.

In certain clinics early operation upon the plexus is advised. This obvious expedient has been thoroughly tried out. The plexus is rather difficult to expose. A blood-stained mass of tissue can be seen. The nerves, more or less frayed out, can be isolated in certain cases. The suture of these fragile tissues is difficult; on the whole, we believe it is not proved that immediate surgical interference is wise in this relatively mild type.

A second possibility is delay for a period of months or years with subsequent orthopedic operation of the type advised by Sever for late cases. Satisfactory as his results are, a waiting policy does seem to us desirable if early well-planned and continuous treatment can be obtained. Tenotomies and osteotomies, in our opinion, are invaluable in correcting the deformi-

ties due to long-standing neglect. They minimize the results of unwise delay, but should not be regarded as ideal. If neither immediate operation nor indefinite delay are approved we are left with the task of early non-operative treatment. The two resources we can make use of consist of apparatus and of exercise. Of the two, exercise is the more important, in our opinion.

The treatment by muscle training of little babies is unquestionably a difficult procedure. First of all we make the situation perfectly plain to the parents. They are told that they may choose between regular attendance, at least twice and preferably three times a week, for an indefinite period, and delay, with the probability of later operation to relieve contracture. Obviously circumstances make regular attendance difficult for many. In this case, however, loyal co-operation is assured.

Our aim is to develop, by active motion, every bit of power in the muscles with defective nerve supply. For a considerable period passive motion may be necessary, but from the very start an effort is made to train the child. Obviously this cannot be done by expecting, at first, the conscious carrying out of orders. The child is, therefore, taught simple games which involve the use of the defective muscles.

These games are based largely on the Poulsson system of finger play and are accompanied by simple rhymes or instructions.

In the first place to educate the child in using the fingers:

"Little birdies in their nest  
Go hop, hop, hop, hop, hop,  
They try to do their very best  
And hop, hop, hop, hop, hop."

While this little verse is sung the fingers of the baby are passively flexed and extended. Very soon the baby will try to move the fingers while the teacher sings; its response becomes an assisted movement. It is surprising to see how soon little babies learn to associate the various movements with the various rhymes.

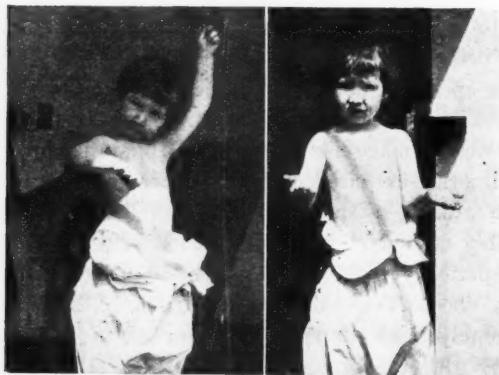


Fig. 161.—Restriction of motion if child had not been treated.

Fig. 162.—Roll over.

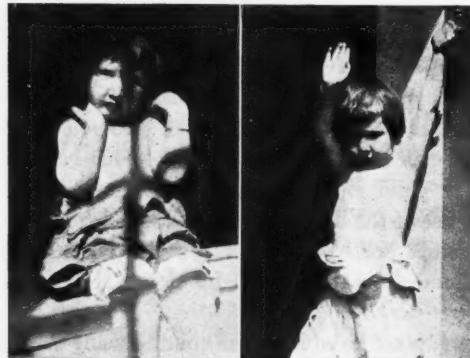


Fig. 163.—Up-down.

Fig. 164.—Ready rocket.

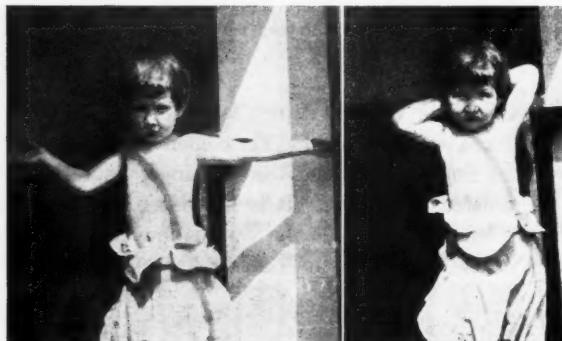


Fig. 165.—One yard of ribbon.

Fig. 166.—Tie a big bow.

Flexion and extension at the wrist are necessary if the child follows the weather-vane motions of the following rhyme:

"This way, that way blows the weather-vane,  
This way, that way blows and blows again,  
Turning, pointing, ever showing,  
How the merry wind is blowing."

By suitable emphasis extension or flexion is made the chief motion.

Supination and pronation are encouraged by:

"Roll over, roll over, so merry and free,  
My playfellows dear, come join in my glee."

The elbow moves in rhythm to the following words:

"Up down, up down,  
This is the way, we go to town,  
What to buy? To buy a fat pig,  
Home again, home again; rig-a-jig jig."

When the triceps is good, we emphasize *up*, and each measure that corresponds to the motion of the biceps. The starting position for the above and also for elevation, abduction, and external rotation is *bend* position. The elbows are bent as far as possible: wrist and fingers slightly bent; hands at side of shoulders (this is contrary to the usual position, but is used to correct internal rotation); arms vertical; elbows close to the wrist.

Abduction at the shoulder is taught by imitating somewhat the old fashioned pump.

"Pump the water, pump the water,  
Pump, pump, pump."

From bend position bring the arm to vertical, with elbow bent at right angle. Holding arm at right angle bring elbow down to the wrist. Repeat six or eight times.

The arm is raised at the command elevation:

"Ready rockets—shoot," the child raising the arm at the last word.  
"Ready rockets—shoot" is repeated six or eight times.

Finally external rotation is obtained by measuring out:

"One yard of ribbon,  
Two yards, three yards,  
And tie a big bow on your hair."

Elbows extended; arms and forearms in a line; palms turned up.

Naturally at the start the motions are entirely passive. However, this preliminary training prevents contractures in some cases. If this simple stretching is insufficient, it is frequently advisable to use a splint for part of each day.

During the whole period of training strict discipline is absolutely essential. On the other hand, it is very evident that short periods will exhaust the very limited powers of attention of the baby. For this reason experience is essential in order to avoid tiring. As the child grows older longer and more vigorous exercises are carried out.

**Case II.**—In order to show the effect of treatment and certain details of procedure, we will now watch a three-year-old girl go through her drill. First she will hold her arm as we think it would have been held without treatment (Fig. 161). As you see, she would have been unable to abduct and externally rotate it at the shoulder and to supinate it at the wrist. After eighteen months' training it is efficient, though certain motions are limited.

**Case III.**—The third patient, who was a neglected case, treated after contractures had become fixed, was operated upon by Dr. Sever. The operation was a fairly severe one and the after-treatment included wearing of the efficient but unwieldy splint, here shown, for a considerable time (Fig. 167).

These cases, which could be duplicated by many others, show a method which is capable of use in other conditions. In essence it is preventive medicine of a useful type. The point which we feel is underestimated by many surgeons is that active co-operation by little babies and by young children is procurable. This method offers an alternative to formidable explorations upon the plexus and to palliative tenotomies, as well as to the

waiting policy which we believe to be based upon misguided assurances that most cases recover without treatment.

Electricity, which is often used with almost child-like faith by certain practitioners as soon as any neurologic disorder is suspected, we have practically discarded in obstetric paralysis. It is quite possible, of course, that its consistent use would be beneficial, but we feel sure that one active controlled motion is worth an indefinite number of passive contractures. Furthermore, active motions can be and should be repeated at home, while electricity in proper doses is available only in the clinic. Obviously, in certain seriously paralyzed cases exploration is justified. Moreover, occasionally training fails to correct con-

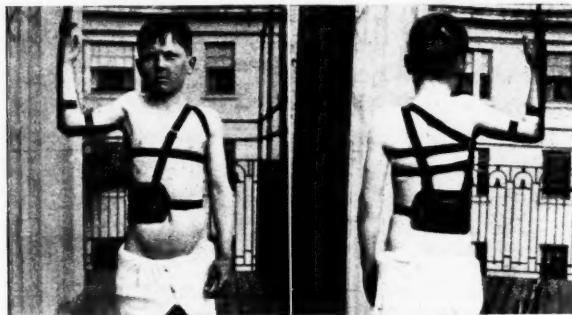
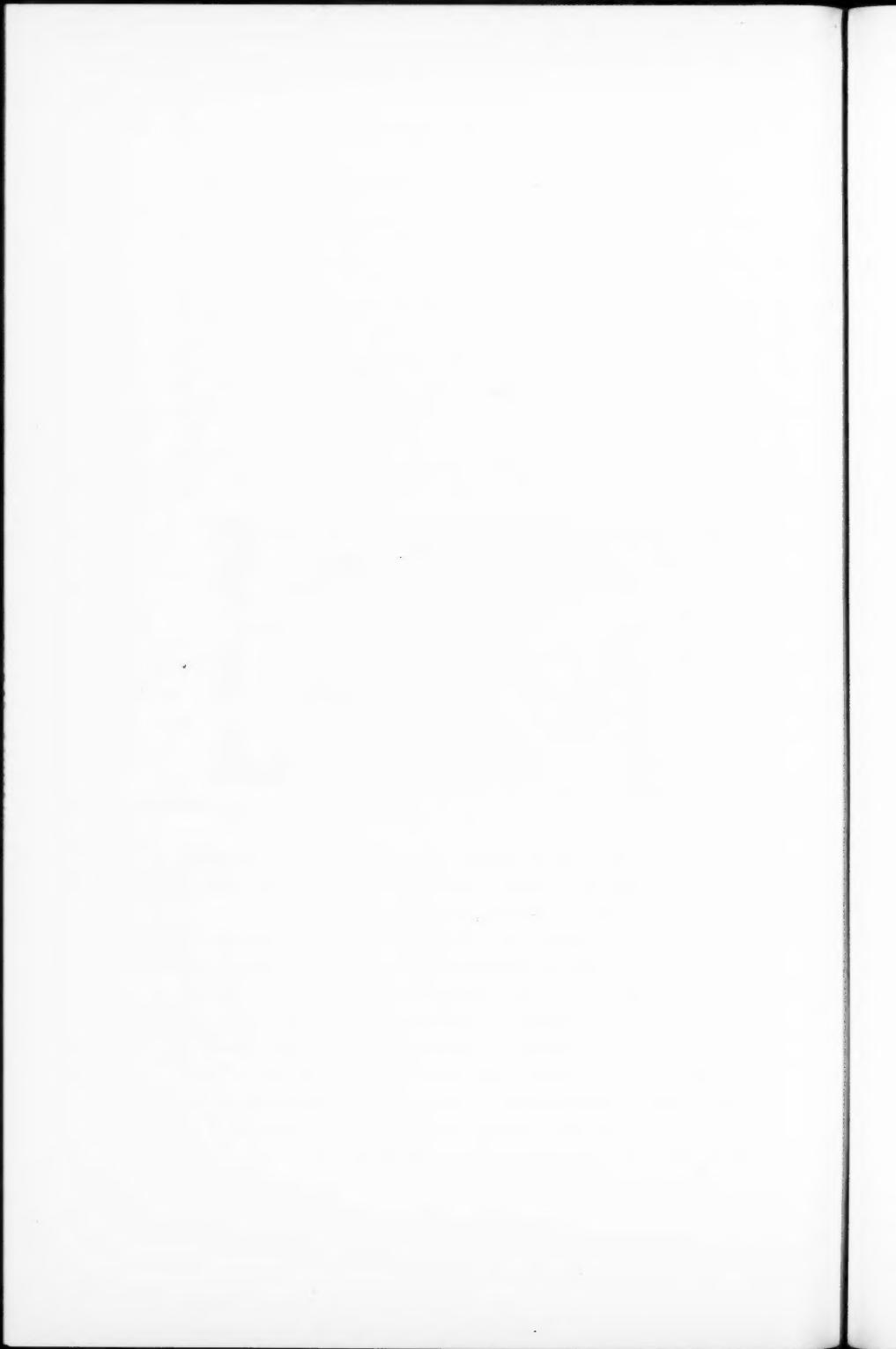


Fig. 167.—Case III. Splints used in passive control of position.

tractures. Operations of various types can then be considered. But the number of children requiring surgery are few and far between if rational and prolonged training is carried out.

This clinic is given not to demonstrate a new method, but to record our belief in and our approval of a method worked out and handed to us by our predecessors, Miss Colby, Dr. Bullard, and Dr. Thomas. It is our hope that this report upon our inheritance of a useful and time-proved method may encourage others to apply kindergarten methods to clinical problems in little children, and to reserve formidable surgical procedures for cases which cannot be treated successfully by a less severe and, we believe, more reasonable plan.



## CONTRIBUTION BY DR. G. O. BROUN

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### TOXIC HEPATITIS FOLLOWING SALVARSAN ADMINISTRATION

OF the various untoward effects of intensive arsphenamin treatment the toxic action on the liver is one of the most interesting and important. The jaundice, which has hitherto been the sole criterion of liver damage, frequently occurs so long after the injection of the drug that the treatment may be pushed beyond the limits of tolerance before the danger-signals are detected. The following cases serve well to illustrate this point and also offer certain suggestions regarding the means to be used for detecting hepatic damage at a less advanced stage.

**Case I.**—The patient is an unmarried man, thirty-two years of age. The past history shows nothing of importance except two attacks of gonorrhea, ten and six years ago respectively, and a luetic infection eight months ago. He has received thirty injections of salvarsan in the past seven months. The last treatment was one month before he entered the hospital. This treatment was followed by a slight immediate reaction in the form of chilly sensations and malaise, but these symptoms quickly disappeared. The patient was actually brought to the hospital by an altogether different condition. About six weeks prior to entry he began having a persistent dry cough. This increased in severity until it kept him awake at night. It became productive, the sputum was yellowish and at times blood streaked. Night-sweats were noted several times. In the interval between the onset of the cough and his entry into the

hospital a loss of 14 pounds in weight was recorded. The patient had grown progressively weaker and for the last two weeks had been unable to work. It was the cough and weakness that brought the patient to the hospital, although he had noticed that his skin had a yellowish tinge for ten or twelve days previous to his entry. About the same time his urine became dark colored. He did not notice the character of his stools. His blood Wassermann reaction was reported negative three months ago.

Physical examination at the time of entry showed a poorly developed, poorly nourished individual, with a distinct yellowish tinge to the skin and conjunctiva. The lungs showed dulness and bronchial breathing at the right apex. Below the angle of the left scapula there was also dulness, harsh breathing, and many fine crepitant rales. The heart showed a soft systolic murmur at the apex, but otherwise nothing of interest. The liver was palpable at the costal margin on deep inspiration. There was generalized enlargement of lymphatic glands. The knee-jerks and ankle-jerks were hyperactive.

*x*-Ray of the chest showed infiltration of the left ascending bronchial tree and obliteration of the left costophrenic angle—probably due to thickened pleura.

The day after entry the blood bilirubin was quantitated by the method of Van den Bergh. The test consists of the comparison of the depth of purple coloration produced in an alcoholic extract of the blood-plasma by the addition of an acid solution of sulphanilic acid and sodium nitrite, with that produced in a similarly prepared mixture containing a known quantity of bilirubin.

In this case 3.5 mg. of bilirubin per 100 c.c. of blood-plasma was found. Normal individuals, in my experience, seldom exceed 0.5 mg. per 100 c.c. plasma, so that in this case we have a concentration of bile-pigment which is about seven times the normal—a well-marked jaundice.

Van den Bergh has also devised a very useful method of differentiating hemolytic jaundice from the other types by the use of this same diazo-reaction. In what he terms the "direct diazo-reaction" the serum or plasma is merely diluted with

two volumes of water and then the sulphanilic acid reagent is added. The time required for the production of a distinct purple coloration is the criterion of the test. If the purple color appears within one minute, the reaction is called "prompt," and indicates a jaundice due to some liver pathology. If the change of color occurs more slowly or not at all, the reaction is "delayed" or "negative." In the presence of increased bilirubin delayed reactions are met with in hemolytic jaundice and allied conditions. Normal sera give delayed or negative direct reactions. The serum of the patient in question gave a prompt direct reaction, indicating the presence of some hepatic lesion.

Another recently devised laboratory method for the study of liver function is the phenoltetrachlorphthalein test of Rosenthal. A known quantity (5 mg. per kilo body weight) of the dye, phenoltetrachlorphthalein, is injected into the blood-stream, and the speed with which the liver is able to remove it is taken as a gage of functional capacity. Normally not more than 5 or 6 per cent. of the dye remains fifteen minutes after the injection, and all should have been taken from the blood by the liver in less than two hours. In the present case at the end of fifteen minutes 16 per cent. of the dye was found in the blood and 14 per cent. was still present at the end of two and a half hours. Distinct impairment of hepatic function was, therefore, indicated.

With the exception of increased quantities of urobilin and some bilirubin, the urine at this time was normal. The stools contained bile-pigments in quantities not appreciably reduced.

The patient was kept in bed for three weeks. During this period there was steady improvement noted in both the pulmonary condition and the jaundice. With the exception of the first two days the course was afebrile. The signs at the left base gradually cleared, the cough lessened, and the patient gained weight. The jaundice lightened considerably and a repetition of the diazo test showed a reduction of the blood bilirubin to 1 mg. per 100 c.c. plasma at the end of the second week. The patient was discharged less than a month after entry. He is still being kept under observation. There has

been no recurrence of the jaundice and the pulmonary condition seems to be progressing favorably. The blood bilirubin is now within normal limits, 0.5 mg. per 100 c.c. plasma. The direct diazo test now gives a delayed reaction. The jaundice has, therefore, completely disappeared.

While this case is complicated by the presence of lung pathology, probably tuberculous in nature, it is nevertheless a typical example of postsalvarsan hepatitis. The fact that there was a considerable interval between the last intravenous therapy and the development of the jaundice is not to be regarded as remarkable, for such delay quite frequently occurs. The degenerative changes in the liver cells do not occur instantaneously, and it is only after a time that they are manifested in an accumulation of bile-pigments in the blood. Cases have been reported in which as much as six weeks elapsed between the administration of the arsphenamin and the development of the jaundice.

The diagnosis in the presence of a history of intensive arsenical treatment is usually not difficult. There is rarely much pain or tenderness in the liver region. In this case and in most that I have seen the liver was slightly enlarged. Bile is usually present in the duodenal contents and stool. Some cases have been reported with acholic stools. These must have been severe cases with practically complete suppression of hepatic secretion. The direct diazo-reaction gives a prompt change of color. This occurs in every case with hepatic damage in my experience, and merely excludes hemolysis as the source of the jaundice.

**Case II.**—Patient is a married man, thirty years of age, and a shoemaker by occupation. One of his children who died at the age of ten months was diagnosed congenital lues. His wife and 3 children are living and apparently in good health. For several years and up to seven months ago he was a heavy consumer of alcohol. He had a definite attack of rheumatic fever at the age of twelve, not followed by any cardiac complications. With the exception of measles and mumps in early

childhood and an attack of "grippe" in 1910 there were no illnesses up to the contraction of the luetic infection. The history of this is not very clear, but the patient believes it occurred in 1915. Treatment was not undertaken until three years ago, when he received several injections of salvarsan over a period of four months. No more treatment was given until December, 1922. He had by this time developed difficulty in walking, awkwardness in the use of his hands, and shooting pains in the arms and legs. He applied for treatment at the dispensary, and between December and April received seventeen injections of salvarsan. Following the last injection the doctors found a trace of sugar in his urine, and for this reason advised his entry into the hospital. There was no polyuria, polydypsia, or polyphagia at any time.

Physical examination on entry revealed entirely normal findings, with two exceptions. The liver edge could be distinctly felt 3 cm. below the costal margin. It was smooth and not tender. The right knee-jerk was absent. At this time no jaundice was perceptible in skin or sclerae.

A faint trace of sugar was found in the urine once after entry, but not thereafter. His blood-sugar was normal. The blood Wassermann reaction was positive. The spinal fluid showed 15 cells per cubic millimeter and a trace of globulin. The Wassermann reaction of the spinal fluid was reported doubtfully positive.

Because of the presence of a palpable liver the Rosenthal test was performed nine days after admission. Liver function was found to be distinctly impaired. Fifteen per cent. of the dye remained in the blood at the end of fifteen minutes, and at the end of three hours 8 per cent. was still to be found.

On quantitating the plasma, bilirubin 1.6 mg. per 100 c.c. was present, a moderate but distinct increase over the normal.

The direct diazo-test gave a prompt reaction.

Prior to the performance of this test jaundice had not been clinically apparent. That it was already developing is shown by the increased blood bilirubin at the time the test was done. Within the next few days an icteric tint developed in skin and

conjunctiva. Bilirubin and increased amounts of urobilin at the same time appeared in the urine. The stools were at no time acholic.

The jaundice increased in intensity for about one week, and then gradually cleared. There was at no time any abdominal pain or tenderness. The liver was readily palpable, but did not increase in size while the patient was under observation.

This case is of interest in that the jaundice developed while the patient was under observation in the hospital. The fact that the liver function test showed well-marked impairment before jaundice was noticeable suggests that we may have here a means of securing early evidence of hepatic injury. It is quite conceivable that the liver enlargement in this case was in some measure due to a pre-existing alcoholic cirrhosis, as there was a definite history of alcoholism. The jaundice, however, was in all likelihood the result of the antiluetic treatment, for the jaundice of cirrhosis is a more chronic affair, this having practically completely disappeared at the time of the patient's discharge from the hospital. The patient was recently seen and shows no clinical signs of jaundice.

**Case III.**—This patient exhibited a more severe degree of liver damage than those previously considered. He is a man forty-five years old. A diagnosis of luetic aortitis was made seven months prior to admission. In that interval he received arsphenamin treatment, ten injections in all having been given. Within a day or two after the last injection his friends noticed his skin was becoming distinctly yellowish. As he was feeling rather tired and weak and had some gripping pains in the upper abdomen he came into the hospital for treatment.

At entry the chief points of interest in the physical findings were: pupils that were equal and regular and reacted to accommodation, but not to light; slightly jaundiced scleræ and skin; a heart enlargement  $12\frac{1}{2}$  cm. to the left of midsternal line, showing a rough systolic murmur in the aortic area and a reduplicated first sound at the apex; the abdomen showed no tenderness or masses, the liver not being palpable.

During the first week after entry the patient seemed to improve, although his abdominal distress was not altogether relieved. At the beginning of the third week he took a rather sudden turn for the worse, marked by increased epigastric pain and great intensification of the jaundice.

The Rosenthal test, performed at this time, showed 18 per cent. of the dye remaining at the end of fifteen minutes, and the even higher reading of 20 per cent. was made at the end of an hour.

On quantitating the blood bilirubin 6.6. mg. per 100 c.c. plasma was found. A prompt direct diazo-reaction was obtained.

The urine showed large amounts of bilirubin, urobilin, and urobilinogen. At this time it contained neither albumin nor sugar. The stools were not acholic.

During the next two weeks the patient was quite ill. The weakness increased, the appetite was poor, and eating caused considerable epigastric distress. The jaundice was very intense, the skin being a deep lemon yellow. There was some tenderness in the epigastrium and under the right costal margin. The liver edge could be felt and seemed soft and flabby. The patient complained considerably of pruritus.

At the beginning of the third week the liver function test was repeated. Functional impairment was still present, but to a lesser degree than the first test had shown. Eight per cent. of the dye was found at the end of fifteen minutes, and 7 per cent. at the end of two hours.

The Van den Bergh test also showed considerable decrease in the jaundice, only 1.1. mg. bilirubin per 100 c.c. plasma being found. The plasma still gave a prompt direct diazo-reaction. The laboratory methods here demonstrated a much greater improvement than was thought to be present, judging from the depth of skin pigmentation and the clinical symptoms.

The history from this time onward is one of slow but steady improvement. He was discharged from the hospital some two months after entry. At this time his blood-pigments were but 0.8 mg. per 100 c.c. plasma, or only very slightly elevated

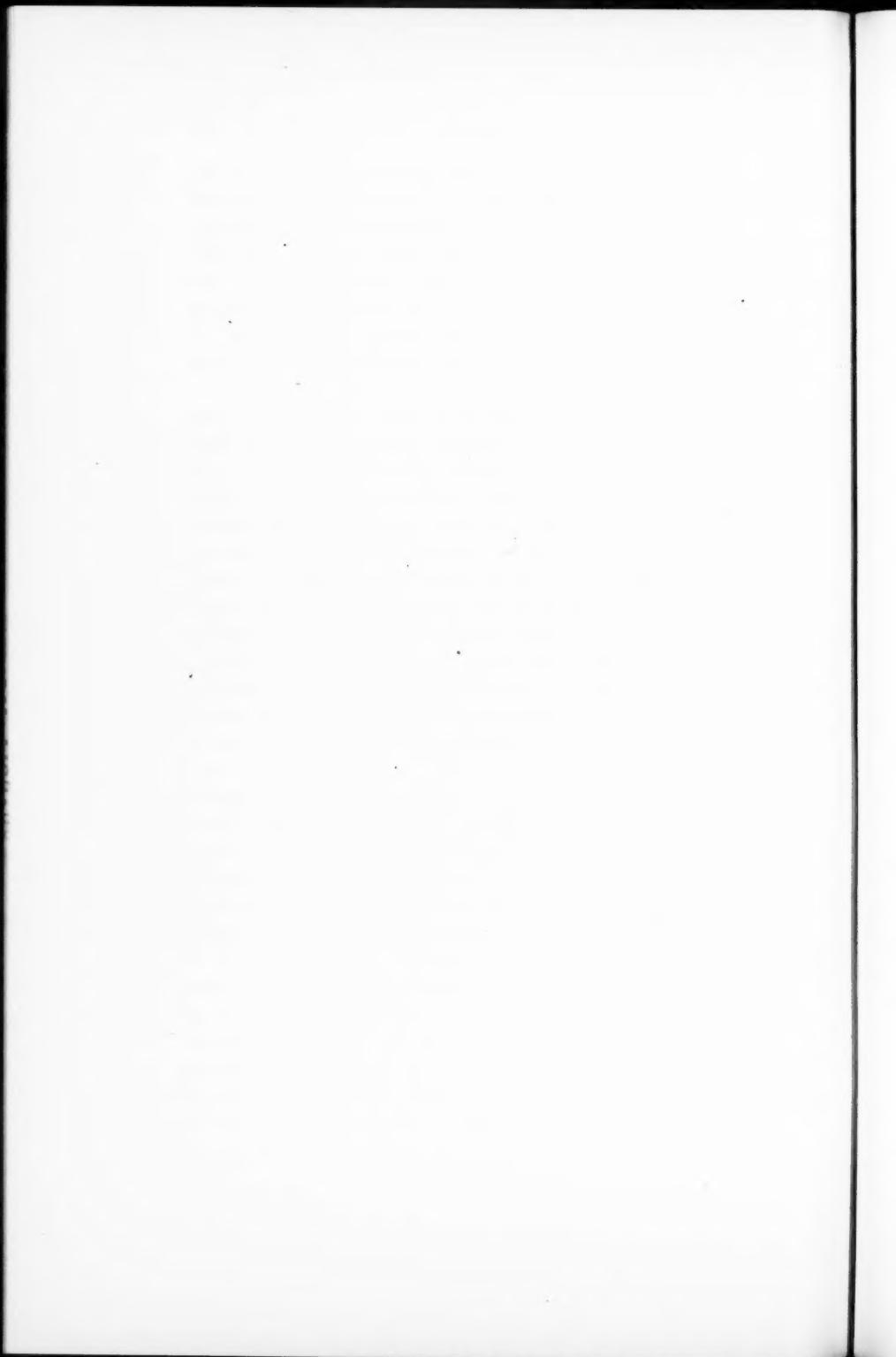
above the normal. There was still some slight coloration of the skin and conjunctiva. His appetite had improved and the epigastric distress had practically disappeared.

This case is illustrative of the severe degrees of liver damage that can be produced by intensive arsenical treatment. At the height of the jaundice the patient was obviously toxic, and an unfavorable outcome was for a time feared. It is well known that fatalities have actually occurred. The value of the recently developed laboratory methods in following the course of the jaundice is well brought out. The fact that improved liver function and decreased blood bilirubin was found on repetition of the tests pointed to a favorable outcome at a time when the prognosis from clinical symptoms and signs was still doubtful.

The pathologic process present in these cases is a degenerative change in the cells of the liver parenchyma, a true toxic hepatitis. Extreme cases may produce the picture of acute yellow atrophy. There is no gross obstruction of the larger bile-ducts, but blocking of some of the smaller bile capillaries by bile thrombi may undoubtedly occur. It is important to note that the stools in the present cases were never acholic, for in catarrhal jaundice or gall-stones acholic stools usually are found at some period in the course of the disease, particularly if the jaundice is intense. Excluding hemolytic jaundice, toxic hepatitis is the one condition in which very intense grades of jaundice are met with in the presence of abundant bile in the duodenal contents and stools. But it is well to remember that a jaundice due to obstruction may persist for some time after the mechanical obstacle has been partially removed. Hemolytic jaundice can be excluded by the use of the direct diazo-test on the blood-plasma. Cirrhosis seldom produces an intense jaundice until it is far advanced, and signs of portal obstruction are usually present to aid in the diagnosis when this stage is reached. Carcinoma also gives little jaundice until the larger bile-ducts are involved in the growth and mechanical obstruction is produced. Then, indeed, the jaundice becomes intense, but with it there is diminution in the bile of the intestinal contents.

There can be no doubt that the diazo-reactions of Van den Bergh and the liver function test of Rosenthal are valuable aids in the study of hepatic disease. They have a place of importance as means of detecting liver damage when jaundice is not yet evidenced by external signs. They give some idea of the severity of the process we are dealing with. And finally, their repetition at proper intervals give us valuable insight into the course of the disease process, enabling us to formulate a more certain prognosis.

It is not unlikely that some slight liver damage may occur with almost every course of salvarsan treatment. We are dealing with an organ that has a large excess of tissue available over and above its actual functional requirements, and which, moreover, possesses to a remarkable degree the power of regeneration in the presence of destructive processes. As not all cases are equally affected by a certain dose of the drug, personal idiosyncracy and the presence of previous liver pathology must certainly play a rôle. It is probably true that no great harm is done as long as the destructive process is held within the limits of the wide margin of safety which the organ possesses. With the assistance of the recently developed tests a more rational method of regulating the intensity of antiluetic treatment would appear to be attainable.



CONTRIBUTION BY DRs. PERCY B. DAVIDSON AND  
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FISTULÆ BETWEEN THE ESOPHAGUS AND THE RESPIRATORY TRACT\*

FROM the standpoint of functional pathology the fistulæ occurring between the esophagus and various portions of the respiratory tract present a number of interesting problems. The recent developments of medical science have resulted in an increasing frequency of recognition of such lesions. Von Richter,<sup>1</sup> in 1792, and Davis,<sup>2</sup> in 1843, were among the earlier physicians to describe congenital tracheo-esophageal fistulæ, a condition now well recognized by obstetricians and pediatricians. Greenhow,<sup>3</sup> in 1874, Arscher,<sup>4</sup> in 1880, and Greene,<sup>5</sup> in 1888, emphasized the rôle of aneurysm of the aorta as a causative factor of esophagorespiratory fistulæ. Tuberculosis was described as an etiologic factor by Heddaeus,<sup>6</sup> in 1889, and Flexner,<sup>7</sup> in 1893. In 1889 a number of instances of varied etiology were classified by Sirot,<sup>8</sup> and the frequency of carcinoma as a basic factor emphasized. The development of a more universal system of postmortem examinations and the diagnosis of many obscure conditions by methods of endoscopy and roentgenology in the last twenty years have pointed out the relatively greater frequency of lesions of this type. The findings at necropsy and the protean manifestations to which they give rise clinically have prompted a review of the literature in the light of the following case recently under observation:

E. I., male, fifty-one years of age, a stereotyper by occupation, entered the fourth medical service of the Boston City

\* From the Fourth Medical Service and the Pathological Laboratory of the Boston City Hospital.

Hospital on April 12, 1923 with the complaint of "difficulty in swallowing." His family history presented no especially interesting points except that one brother died of tuberculosis early in the patient's boyhood. His past history brings out the following positive points: Diphtheria at ten, gonorrhea at eighteen, excessive alcoholism since youth; a stereotyper for twenty-five years in constant contact with lead fumes; vague chest pains for the last three years, occasional indefinite headaches, substernal pains for the past two years not radiating to left arm or confined to precordium, and chronic constipation. He dates the onset of his present illness to January 1, 1923, at which time he noted loss of weight incompatible with his general feelings of well being. He consulted his family physician, who told him that he was "run down" and advised a vacation. After a rest of two weeks he attempted to return to work, but was unable to do so owing to his general loss of strength. Late in February, for a period of about a week, he noticed difficulty in swallowing any but liquid food. When put on such a diet he was fairly comfortable for about three weeks. Then his condition became progressively more distressing, characterized especially by "gas in stomach" and precordial pain, both somewhat relieved by belching. Late in March the patient had a chill, accompanied by pain in the chest, radiating around to the shoulders. The family physician saw him two days later and diagnosed "pneumonia"; the crisis is said to have occurred five days afterward. As a sequel of this illness the patient had a cough productive of large amounts of mucopurulent sputum, tinnitus, and hoarseness, all of which had persisted up to and subsequent to admission to the hospital.

For six weeks preceding admission swallowing had become progressively more difficult, and he was finally able to take food only by drops. The last three weeks of this period vomiting, accompanied by coughing at practically every effort to take food, had been a feature; blood-streaked sputum was noted at this time, but frank hemoptysis did not occur until four days before admission.

Physical examination on admission showed the following

positive findings: marked emaciation, rapid shallow respiration, diminished movement of left chest, dulness of percussion note over both apices, harsh breathing over apices, friction-rub in right axilla, coarse and medium moist râles throughout right lower lung and in left chest from the apex down to fourth rib, diminished vocal fremitus over entire left base, and hard small glands palpable in cervical triangles.

The patient was fluoroscoped the same afternoon, and in the recumbent position showed shadows over both apices, with one of greater density in the second interspace near the sternum. The costophrenic angle on the left was obscured; on the right it was clear. The diaphragm moved on both sides with respiration, but movement was restricted on the left. There was a peculiar blurring of the lower portion of the left chest. The abdomen showed nothing unusual.

The patient was now observed in the esophageal position. A shadow was seen in the posterior mediastinum at a point corresponding to the level of the bifurcation of the trachea. A thin barium mixture was then fed, only small sips of which were possible due to the discomfort therefrom. The swallowing reflex was apparently normal. The bolus was interrupted in its passage at a point somewhat above the level of the bifurcation of the trachea. Here moderate dilatation was noted and the barium ran out in fine lines, which increased in size (Fig. 168). An irregular filling defect was noted in the esophagus below the dilated area, through which barium passed, to continue on its passage to the stomach without obstruction. When the patient was again placed in the recumbent position the bronchi of the left lung appeared filled with barium (Fig. 169). Plates taken at this time in the main confirmed the fluoroscopic examination, but showed, in addition, barium in the right primary bronchus.

As a result of the clinical and the Roentgen pictures the diagnosis of tracheo-esophageal fistula secondary to carcinoma of the esophagus was made. A traction diverticulum secondary to tuberculous glands was considered on account of the clinical findings at the apices and the Roentgen findings in the lungs

and posterior mediastinum. Fluid in the left pleural cavity was considered, but could not be confirmed by *x*-ray, owing to the inadvisability of fluoroscopy in the erect position. The shadow in the left second interspace was thought to represent a lung abscess.

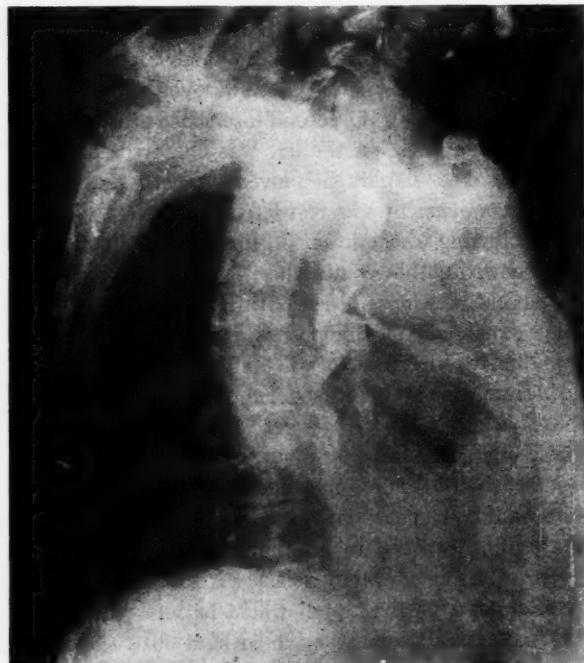


Fig. 168.—Roentgenogram in oblique position showing barium in the esophagus and bronchi.

In view of the grave condition of the patient a gastrostomy was thought advisable immediately. This was done under local anesthesia by Dr. F. C. Lund on April 19, 1923. The patient's general condition grew steadily worse and death occurred on the fourth day after the operation.

The positive findings at autopsy were: Marked emaciation, recent operative scar in upper abdomen with tube leading to

pyloric antrum, the left pleural cavity completely obliterated by dense fibrous tissue, except at the base, where a small cavity remained. Upon opening the esophagus the explanation of the clinical picture was evident. At a point opposite the hilæ of the lungs on their anterior and lateral aspects was an ulcerating fungating tumor mass measuring 8 by 5.8 by 4 cm. Its edges were irregular, indurated, and sloped down to an uneven gray

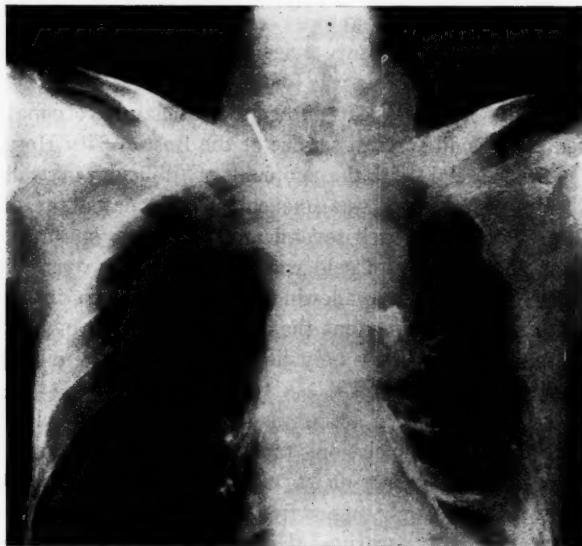


Fig. 169.—Roentgenogram in anteroposterior position showing barium filled right and left bronchi.

friable base covered with lumps of barium. Here and there deep fissures led down to adjacent tissues, one of which, 0.5 cm. in diameter, opened into the trachea on its left side just at its bifurcation, where lumps of barium had collected. Another opening, 0.8 cm. in diameter, led into the substance of the left lung just above the hilum, where a cavity 4 cm. in diameter had formed. The walls of this cavity were reddish purple and apparently lined by necrotic lung parenchyma. Just above the

tumor mass the esophagus was somewhat dilated, and on its anterior wall, for a distance of 3 cm., were a number of hard grayish-white nodules, in size up to 0.5 cm. in diameter. Microscopic examination showed carcinoma of the epidermoid type of the esophagus. The anatomic diagnoses were: Carcinoma of the esophagus with esophagotracheal and esophagopulmonary fistulae, chronic pleuritis with atelectasis of the left lung, and recent gastrostomy.

In looking over the autopsy records of the Boston City Hospital for the past twenty-five years only one other case of esophagorespiratory fistula was found.

D., male, forty-two years of age, a musician by occupation, entered the second surgical service of the Boston City Hospital on December 1, 1900 with the complaint of "difficulty in swallowing." His past history was uneventful. He dated the onset of his present illness back several months, when, one morning following the drinking of cold water while he was overheated, he noted difficulty in swallowing. This dysphagia increased in severity to such an extent that for the past two months he had been able to swallow only liquids. Bougies were passed, with only temporary relief.

Physical examination on admission disclosed the following positive findings: emaciation, tachycardia, hyperpyrexia, labored respiration, coarse moist râles throughout both lungs, especially over the right upper front. Laryngoscopic examination was essentially negative. His course in the hospital was characterized by dysphagia, dyspnea, cough, tachycardia, and hyperpyrexia.

The positive findings at autopsy were: emaciation, left pleural adhesions, discrete and confluent areas of consolidation in lower lobes, mucopurulent material, with odor of gastric contents in bronchioles. In the middle third of the esophagus the wall was much thickened for a distance of 5 cm. In this situation the inner surface was a dirty white color and very friable. A ragged opening in the anterior wall, 2 by 2 cm., led into the trachea on its right anterolateral wall, just above the exit of the primary bronchus. On section, the normal esophagus

merged sharply into the thickened zone. Between the esophagus and trachea was an elongated flattened mass, which, on section, was similar to the thickened esophageal wall, with which it was continuous. On the anterior wall of the esophagus, 5 cm. above the upper limit of the tumor, was a raised yellowish-white nodule, 0.5 by 0.8 cm. Just below this was a similar but smaller nodule. On the left anterolateral wall of the trachea, just above its bifurcation, was an elevated area, 4 by 2 cm.; its surface was dirty white, uneven, and friable. At the site of the opening of the fistula was a similar but smaller nodule. The anatomic diagnoses were carcinoma (epidermoid) of the esophagus with tracheo-esophageal fistula, metastases to trachea, and bronchopneumonia.

**Pathology.**—In studying the fistulous passages between the esophagus and respiratory tract it is essential to have a clear idea of the histogenesis of these structures and their exact relations to each other and to adjacent organs. It will be remembered that the respiratory system begins as an outgrowth from the entodermal alimentary canal in its esophageal portion by the formation of a longitudinal median groove on its ventral wall. As this groove deepens, its edges approach, fuse together, and the groove is converted into a tube which is gradually separated from the esophagus, beginning at the end toward the stomach, progressing upward to the pharynx. Even before the constricting off of this tube or pulmonary diverticulum is completed, its free end bifurcates, and here the lungs take their origin. Later, canalization of this tube takes place. It is evident then that failure at any point to pinch off completely would leave the pulmonary diverticulum still in communication with the esophagus, and when canalization took place a fistula would be formed. Thus, many different congenital malformations are possible.<sup>9, 10</sup>

Under normal conditions in the adult the esophagus maintains a position directly posterior to the trachea and in apposition with it, from the origin of the latter to its bifurcation. Here it courses slightly to the left, passing behind the left bronchus. The two structures are separated only by occasional

lymph-nodes, the most important of which are found at the bifurcation. Below this the pericardium and the diaphragm lie anterior. Posteriorly are the prevertebral fascia and the bodies of the vertebrae, until it reaches the level of the sixth thoracic body, when the aorta and right vagus, which have occupied the left lateral position, gradually come to lie directly between it and the bodies of the vertebrae. Its lateral relations in the neck are the recurrent laryngeal nerves and the contents of the carotid sheath. From the level of the third thoracic vertebra the pleura comes to lie on its lateral aspect and continues to do so throughout.<sup>11</sup> Thus, lesions attacking any of these structures may involve others, and whenever ulcerative changes take place intercommunicating fistulous tracts are likely to occur.

The conditions which lead to fistulae to and from the esophagus may be conveniently enumerated according to their frequency of occurrence. Carcinoma, so far as can be ascertained, is the only new growth giving rise to esophagorespiratory fistulae.<sup>12,13</sup> Although secondary involvement from cancers of the stomach, pharynx, thyroid gland, and respiratory tract, or metastases of these to mediastinal glands may occur,<sup>14, 19</sup> yet the majority are the sequelae of primary cancer of the middle third of the esophagus.<sup>15, 16</sup> Fistulae secondary to malignancy in the upper third and at the cardia are rare; in the former location cancer is relatively infrequent, whereas in the latter, a favorite site, the anatomic relations do not predispose to fistula formation. In the middle third, as has been pointed out, the esophagus, trachea, left bronchus, and pleura are intimately associated. Moreover, negative pressure in the pleural cavity may play a rôle as a predisposing factor, especially during deglutition, when the pressure within the esophagus is increased. Indeed, Ewald<sup>17</sup> affirms that as high as 50 per cent. of carcinomata in the middle third of the esophagus form esophagorespiratory fistulae. In 20 cases, of which 12 were in the middle, 1 in the upper, and in the lower third, coming to autopsy at the Boston City Hospital, only 2 showed this complication. Of the two types of carcinoma which primarily involve the esophagus, the squamous-cell variety leads to most of the fistulae. Adenocarcinoma tends

to infiltrate, obstruct, and ulcerate, but is infrequent.<sup>13</sup> In our series of 20 cases, only 1 was of this type. Squamous-cell cancer in this location is usually medullary in character, consequently necrosis and ulceration are found with great regularity. The more scirrhous type does occur, however, and in these fistulæ are less common. A very scirrhous carcinoma, similar to that of the stomach, which masquerades under the title of *limitis plastica*, is occasionally seen. One such case came to necropsy here a few years ago; the lower third of the esophagus and the cardia of the stomach were diffusely infiltrated, yet without ulceration or extension to adjacent organs.

The point of ulceration into the respiratory tract is most commonly into the trachea at or just above its bifurcation; the left bronchus, as would be expected, is more commonly attacked than the right.<sup>15, 18, 20</sup> After the fistulous tract has formed, pulmonary complications, such as pneumonia,<sup>15, 16</sup> abscess, gangrene,<sup>21</sup> and secondary tumor nodules rapidly set in, leading to early death. When the tumor extends in a lateral direction involvement of the pleura and extension into the lungs is rapid.

Congenital malformations are probably responsible for the second largest group of esophagorespiratory fistulæ. Their presence indicates an arrest of development, giving rise to different types, depending upon the stage attained. Commonly, the main bronchi are found to open into the lower half, while the upper portion of the trachea opens below into a blind sac.<sup>22, 23, 24, 25, 26, 2, 10</sup> All gradations from this have, however, been reported.<sup>27</sup>

Tuberculous fistulæ occur mainly in children, although adults are not exempt. Peritracheal and peribronchial lymph-nodes attached either primarily or secondarily to lesions in the respiratory tract, discharge their cancerous contents usually first into the trachea and then into the esophagus.<sup>6</sup> The so-called "bifurcation gland," which is in such close contact with both structures has been many times the offender.<sup>28, 29</sup> Whether fistulæ result directly from primary tuberculosis of the trachea or bronchi is a matter of doubt. Tuberculosis primary in the

esophagus is said never to occur.<sup>12, 30</sup> Now and then ulcerative processes in the lung itself extend through the pleura to involve the esophagus directly.<sup>31, 32</sup> Multiple tuberculous ulcers of the intestine, as a rule, terminate the disease,<sup>29</sup> but empyema<sup>7</sup> and miliary tuberculosis are sometimes lethal agents.

Syphilitic fistulae are the result of two tertiary manifestations of the disease. Gummatus infiltration of both the esophagus<sup>33, 34, 35</sup> and air-passages<sup>34, 36</sup> is not uncommon. Any portion of the esophagus may be attacked, but in the respiratory tree the lesions are usually at the larynx, decreasing in frequency of occurrence from above downward; the bronchi are a very rare site. Necrosis and ulceration take place rapidly, and large masses of tissue, such as rings of the trachea, may become separated at one time.<sup>36</sup> Perforation and fistulae, as would be expected, commonly result. Aneurysms, on the other hand, are a rare cause of esophagorespiratory fistulae. The fistulous tract may extend directly through the aneurysmal sac by erosion or be simply the result of pressure.<sup>37, 3, 4, 5</sup>

Inflammation of esophagus is commonly the result of chemical and thermal agents in ingesta or of foreign bodies,<sup>38, 39, 40</sup> and rarely of extension of an inflammatory process from the pharynx or stomach. That type which may give rise to various complicating conditions is phlegmonous or diffuse suppurating esophagitis. It may be secondary to a suppurating focus elsewhere, such as the lung or pleural cavity,<sup>41, 42</sup> but may follow directly the action of foreign bodies or corrosive substances. Beginning in the submucosa, purulent infiltration rapidly spreads, undermining the mucosa and extending through the muscular coats. Thus pockets of pus are formed which may rupture into the trachea, pleura, or mediastinum.

A rare and interesting type of esophagorespiratory fistulae is that due to esophagomalacia.<sup>43</sup> It occasionally occurs as an agonal manifestation in cases of cerebral disease in consequence of digestion of the esophageal wall by gastric contents. Probably, in the majority of cases, the process is postmortem.

Actinomycosis<sup>44</sup> and esophageal diverticula<sup>45</sup> may be unusual causes of esophagorespiratory fistulae.

**Clinical Picture.**—The consideration of the varied pathology which may form the basis of fistulæ between the esophagus and respiratory tract impresses one with the futility of seeking a definite clinical picture. However, there are certain concomitant symptoms which should arouse suspicion regarding the existence of such a condition, independently of those which may be interpreted as associated with basic disease. One may conveniently divide a discussion of general symptomatology of esophagorespiratory fistulæ into those occurring congenitally and those acquired after birth.

The symptom-complex of congenital esophagotracheal fistulæ is a very definite one. The first matter to attract attention is the inability of an otherwise apparently normal child to nurse. It may suckle for a while and then become extremely cyanotic and dyspneic,<sup>24, 46</sup> immediately coughing up the food. The close association with other developmental defects, such as atresia<sup>2, 22</sup> of the anus, may at first divert attention to these obvious conditions, but soon the nursing and respiratory difficulties become apparent and the child dies within a few days of birth, usually from associated intercurrent infection, as pneumonia,<sup>33</sup> or from inanition.

The picture of fistulæ acquired later in life is, however, a more indefinite one.<sup>47</sup> The patient usually gives a history of dysphagia for varying lengths of time preceding the illness, which gradually increases in severity until the onset of pulmonary complications. At this time it is noted that dyspnea, profuse purulent expectoration, hemoptysis, and cough immediately after the ingestion of food occur. The patient may consult the physician principally because of the pulmonary aspects of the condition, keeping the digestive factors in the background. The first indication of such a fistulæ, on the other hand, may be the onset of pneumonia or lung abscess clinically or their discovery at the autopsy table. In most cases it is usually necessary to resort to special methods of examination.

Roentgen and esophagoscopic examinations are now responsible for the large number of antemortem diagnoses of the conditions. Careful fluoroscopy, utilizing a thin suspension of

the opaque salt, is not associated with much danger and will yield the most satisfactory results. It will demonstrate the extent of normal passage of the meal along the esophagus, the type of obstruction (whether regular, irregular, sacculated, or apparently due to external pressure), and the point of communication with the respiratory tract.<sup>48, 49, 50, 51, 52</sup> An esophagoscopic examination<sup>18</sup> in the hands of an expert will give most valuable information, but for routine procedure it is not as feasible or relatively safe as the Roentgen method, though, in cases in which the etiologic factor is not apparent after careful roentgenoscopy and where a foreign body may be encountered and successfully removed, it may be the method of choice.

If these cases are ever to be satisfactorily handled, it is necessary not only to diagnose the peculiar morphologic alteration but also the basic disease. This can be done only by careful consideration of the pathologic peculiarities of the disease in question, the anatomic factors of contiguity, and the array of symptoms to which pathologic conditions give rise.

Carcinoma, the most frequent single cause of esophago-respiratory fistulæ, presents a varied symptomatology. The symptoms may be predominantly digestive,<sup>53</sup> with marked dysphagia, subacutely respiratory,<sup>54, 15, 18, 48</sup> with dyspnea, purulent expectoration, hoarseness, hemoptysis and profuse involvement of the lungs (on x-ray and physical examinations), or acutely respiratory,<sup>15, 52, 53, 55</sup> with the picture of pneumonia, as the prominent feature. Our cases, both having primary carcinoma of the esophagus, were characterized primarily by dysphagia, with respiratory symptoms as relatively late complications; this is probably the more usual picture. Numerous observers have reported instances of primary carcinoma of the esophagus in which respiratory symptoms were the feature without any particular previous incrimination of the digestive tract. Cases have been reported in which bronchopneumonia was the primary diagnosis and esophagorespiratory fistulæ but were incidental findings at postmortem.<sup>15, 16, 50</sup> The age of the patient (in the cancer period), sex (most frequent in males), negative antecedent history, recent dysphagia with much more

recent respiratory symptoms<sup>56</sup> should arouse suspicion of the existence of esophagorespiratory fistulae of carcinomatous origin. The large proportion of cases not showing the usual line of symptoms should, at the same time, not be an indication for neglecting fistulae in dealing with varied types of respiratory disease.

As primary tuberculosis of the esophagus practically never exists, it is to the group of symptoms accompanying involvement of the bronchial lymph-nodes<sup>6, 28, 29</sup> and the lungs<sup>31, 32</sup> that one must look for the establishment of such an etiologic basis. Dysphagia, dyspnea, and orthopnea are localizing manifestations in a tuberculous broncho-adenopathy, especially when accompanied by the systemic reactions to tuberculous infection, such as intermittent pyrexia, noctidrosis, and fatigability; when such a group of symptoms is augmented by the more recent onset of cough immediately after the ingestion of food, profuse expectoration, and increasing dysphagia, the establishment of fistulae between the esophagus and respiratory tract must be considered. Other broncho-adenopathies must be carefully excluded by a consideration of the general clinical pictures of these conditions, and special laboratory studies of the blood and of glands, excised from some other part of body. The onset of dysphagia, markedly increased expectoration, paroxysms of cough immediately after eating, or of symptoms of acute pneumonia in an individual with local and general evidences of pulmonary tuberculosis, should lead to the suspicion of the existence of fistulous tracts to the esophagus from the lungs. In a consideration of any individual case tuberculosis must be considered as accounting for the general as well as the local symptomatology.

Medical practice, in its avidity for the assignment of a luetic basis for most diseases, has not ignored esophagorespiratory fistulae. A positive history of luetic infection and confirmatory laboratory data may be helpful in many cases, but may be distinctly misleading when one realizes the incidence of lies. These tertiary lesions largely occur in early middle life. The fistulae occurring in the course of aneurysm of the aorta may be

accompaniments of the so-called "aneurysms of signs" and "aneurysms of symptoms."<sup>37, 3, 5, 4</sup> The usual association of hoarseness, brassy cough, tracheal tug, dysphagia, pupillary and pulse inequalities, and dyspnea may precede such signs of involvement of the respiratory tract as acute symptoms of pneumonia, or the profuse expectoration occurring with pulmonary abscess or gangrene, and paroxysms of cough after eating. The classical signs and symptoms may be absent at first and become apparent only at the onset of the digestive and respiratory complications of the fistulæ. The symptoms accompanying fistulæ subsequent to gummata are dependent largely on whether the respiratory tract, the esophagus, or the mediastinal lymph-nodes are primarily involved. In those cases in which the involvement is primary in the trachea or bronchi, dyspnea is an early and marked symptom, being augmented by the complex of dysphagia, paroxysmal cough after eating, and pulmonary complications when erosion has taken place into the esophagus.<sup>36, 67</sup> When the esophagus is primarily involved, dysphagia is the early marked symptom and is followed later by cough after eating, dyspnea, and pulmonary symptoms.<sup>34, 35</sup> When the mediastinal glands are the seat of earliest involvement the symptoms may be very much like those accompanying aneurysm, but can be differentiated by careful Roentgen study; here again the formation of fistulæ is accompanied particularly by pulmonary manifestations, though dysphagia may be an early symptom.

Inflammation of the esophagus, through extension along its lumen or from the periphery, giving rise to fistula formation, presents varied clinical pictures dependent largely on the etiologic factors. The history of swallowing foreign bodies, such as a denture<sup>31, 39</sup> or the plaything of a child, though rarely recorded, leads to the recognition of one of the most frequent inflammatory causes of fistula formation. The symptoms may be those merely of dysphagia, followed later by dyspnea, cough after eating, profuse expectoration, and occasionally of acute pneumonia; here, more than in any other condition, the esophagoscope may be of great value in diagnosis. The clinical picture

of fistulæ following empyema may be that of an early pneumonia followed by empyema and fistula formation, or may be unaccompanied by any preceding history of empyema and be very insidious.

The clinical picture of esophagomalacia<sup>43</sup> has been ignored by clinicians due to the fact that the postmortem findings were invariably interpreted as occurring after death. The patient is usually moribund in the course of some infection and presents as most marked symptoms hematemesis and dyspnea, the latter of which probably is coincident with the rupture into the pleural cavity.

Diverticula, both pulsion and traction, may lead to fistulæ into the air-passages. The history is usually one of dysphagia for a relatively long time, followed, with the establishment of the fistula, by the respiratory symptoms of cough after eating, dyspnea, profuse expectoration, and hemoptysis. Symptoms suggesting the involvement of the mediastinal glands, which might give rise to the traction diverticula as well as the location of the esophagus in which the diverticulum occurs (pulsion usually in the upper third), will be of value in determining the type of diverticulum present.<sup>44</sup>

The differential diagnosis of esophagorespiratory fistulæ from the etiologic standpoint may be a difficult one. Age is a factor which may be helpful, for it is known that carcinoma usually occurs in middle life or later, that very active tuberculosis, especially the glandular type, is a disease of early life, that swallowing of foreign bodies is most common in children, that tertiary lues presents its most active manifestations years after the primary infection, and that diverticula can occur at practically any age. While the majority of reported cases have been in men, it seems unlikely that the sex factor can be considered as significant. Since primary carcinoma is the most frequent single cause in adult life, its diagnosis should be carefully excluded before assigning any other etiologic factor.

**Treatment.**—Modern methods of medical treatment and thoracic surgery have lifted from utter hopelessness many diseases of the lungs and esophagus. Carcinomata of the esophagus

gus have been operated upon, usually with very little success, and offer practically no hope for the eradication of the neoplasm. In these cases gastrostomy alone is the surgical procedure for the prolongation of life, though one gets the impression from our own and the reviewed cases that the prolongation, usually extending not over a week, is not worth the discomfort of operation. Congenital fistulæ offer no hope from operative procedure, because of the age of the child and the usual concomitant malformations. Aneurysms are at present hopeless from the medical and surgical aspects. Gummata of the trachea, lymph-glands, and esophagus will respond to antiluetic therapy, but even here its advisability is under question because of the possible extensive resolution of gummata and the consequent increase in size of fistulæ.<sup>55, 34, 36</sup> Extensive tuberculosis, of both lungs offers no prospects for therapy, while involvement of one permits the utilization of pneumothorax on the affected side in an endeavor to prevent aspiration into the lung and close off the fistulous opening. Tuberculous lymph-nodes will sometimes respond to Roentgen therapy, and treatment should be attempted, but the usual presence of complications precludes very bright prospects. Diverticula of the pulsion type, which are usually situated high in the esophagus, respond to surgery. The best results may be obtained in those cases secondary to foreign bodies; removal of the object through the esophagus will sometimes in itself effect a recovery, while the addition of a temporary gastrostomy may assist the healing process.

**Summary.**—1. Two cases of esophagorespiratory fistulæ subsequent to carcinoma of the esophagus are reported.

2. The varied pathology at the basis of esophagorespiratory fistulæ is discussed.

3. The cardinal symptoms of fistulæ in general and those peculiar to specific pathologic lesions are brought out.

4. The possibility of treatment of fistulæ is outlined, both as regards methods and effectiveness.

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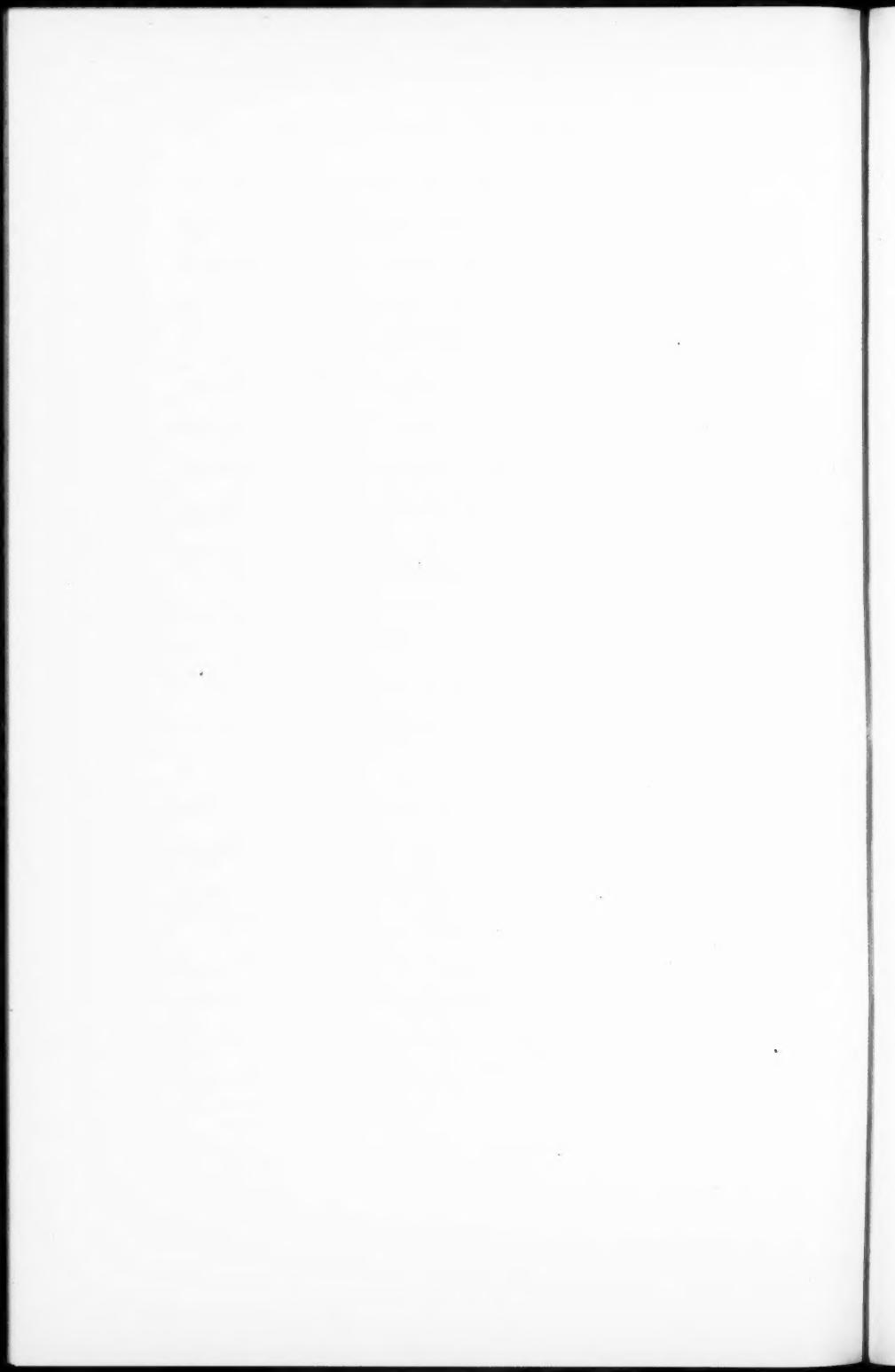
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## CLINIC OF DR. F. B. GRANGER

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### PHYSIOTHERAPY

PHYSIOTHERAPY has been practised since the beginning of the world, yet was born in the World War. Prior to that time the various branches of physiotherapy were being developed each in its little narrow groove. With the advent of the war and the necessity of returning men more speedily to the front line, it became imperative to use, as an adjunct to all other branches of medicine and surgery, all types of physical therapeutics either singly or in combinations. In the United States this unification was consummated by the Surgeon-General of the United States Army, when he created the Department of Physical Reconstruction, and defined physiotherapy as "Physical measures such as are employed under the term 'physiotherapy,' including hydro-, electro-, and mechanotherapy, active exercises, indoor and outdoor games, and passive exercises in the form of massage." The success obtained in the army stimulated civil hospitals, insurance companies specializing in occupational injuries, and large employers of labor to establish such departments. The Boston City Hospital long before the war had realized the value of such measures and had had for a number of years a Department of Physical Therapeutics in full operation. Cases of many varied types are referred for treatment from practically every department in the hospital. The following pathologic conditions are a fair index of their variety.

### PERIPHERAL FACIAL PARALYSIS

Peripheral facial paralysis is amenable to treatment. Untreated, many cases recover, but, as a rule, the paralyzed muscles

are forever after weaker than normal. Also without treatment the duration of disability is prolonged to months instead of weeks. The partial etiology of this pathologic condition, enumerated in the order of frequency, is:

1. Refrigeration. This is supposed to be due to chilling of the nerve with consequent inflammation and degeneration. My own feeling is that such types are really due to infection (similar perhaps to that seen in herpes zoster) or they may be associated with sinusitis.

2. Postoperative (after mastoiditis). This varies from section of the nerve (in which a nerve anastomosis is the only chance of cure) to mechanical compression of the nerve; or to degeneration due to some infective process, or, as an end-result, to pressure caused by cicatricial contraction somewhere along the bony channels in which run various branches of the facial nerve.

3. Traumatic. This may occur after head injuries such as fracture of the skull, etc. As a rule most cases may be grouped in Class 1, or in the second section of Class 2.

The treatment depends on two factors:

1. The character of the pain.
2. The degree of nerve degeneration.

In many good text-books the statement is made that physiotherapy, especially electrotherapy, *may* be of value *after* the painful stage has passed. This is erroneous, as not only are the results much better the earlier the treatment is instituted, but by the rapid amelioration of pain the patient is spared much suffering.

No prognosis should be given until ten days after the onset of the paralysis. Usually at that time the degeneration has reached its maximum. This does not mean that treatment should be omitted during this period, but rather that certain procedures which may be of value should be held in abeyance during this interval.

In general, the treatment is as follows: If there is much pain, positive galvanism, for its sedative effect, is employed over the painful area, while, conversely, if there is little pain,

negative galvanism, for its stimulative properties, is indicated. Next, some form of electric stimulation is necessary; the particular type depends on the degree of degeneration and the time that has elapsed since the onset of the attack. During the first ten days interrupted galvanism only should be used, the polarity depending on which pole gives the greater mechanical response. For example, with a complete reaction of degeneration, use the positive pole. With an incomplete reaction, use the negative. After ten days employ that type of electricity which will give the greatest degree of muscular contraction with the smallest amount of current. This may mean the Bristow faradic, the slow sinusoidal, or the interrupted galvanic. The moment the muscles show signs of tire, as evidenced by lesser amplitude of contractions, stop the treatment, whether 3 contractions or 50 have been produced. It is important in all types of peripheral paralysis not to tire the musculature, as harm may thereby result. Later, massage for its nutritional effect and re-educational exercises are of value.

**A Typical Case.**—The exact technic of a typical case is as follows: Determine the degree of degeneration by

1. Faradic reaction. Test the unaffected side and note the amount of faradism necessary to cause a vigorous contraction. Test the affected side. Does it respond to the same amount of current? Is more necessary? And finally, does it fail to respond?

2. Galvanic reaction. Repeat as in faradism—only carefully observe if the reaction is slowed (that is, if the contraction of the muscle is slower and more "worm-like"). Determine what pole causes the greater contraction (normally the negative pole should). If the positive pole gives the greater contraction, we have a complete reaction of degeneration.

From these tests we can determine the degree of degeneration present; the probable duration of the paralysis and the proper treatment to be prescribed. The following table (after the tenth day) will give an idea of what may be deduced:

1. Quantitative loss to faradism. (It takes more of the faradic current, but the muscle contracts.) Duration of dis-

ability—four to six weeks. Treatment—Bristow coil or slow sinusoidal.

2. No response to faradism. Galvanic reaction normal. Disability—six to ten weeks. Treatment—negative galvanism for twenty minutes, followed by interrupted galvanism, negative pole.

3. Quantitative loss to galvanism, negative pole giving greater reaction, associated with slowing of muscle contraction. Disability—ten to sixteen weeks. Treatment—negative galvanism for twenty minutes, followed by interrupted galvanism, negative pole.

4. Reaction to both positive and negative poles equal. Duration—sixteen to thirty weeks. Treatment—negative galvanism for twenty minutes, followed by interrupted galvanism, negative pole.

5. Positive pole gives greater reaction. Duration—thirty to fifty-two weeks. Treatment—negative galvanism for twenty minutes, followed by interrupted galvanism, positive pole.

Suppose the given case falls in Class 4 of the above table, and that there is little pain present. The treatment should be as follows:

1. Heat. This may be radiant heat or diathermy. The object is to heat the musculature; improve nutrition by the local active hyperemia induced; relax muscular tissue, and lessen the resistance of the skin. If radiant heat is used, it should be continued to the point of reaction, as evidenced by reddening of the skin. If pain is a factor, diathermy is of value.

Diathermic technic; cover with a large metal pad the entire unaffected side of the face, first thoroughly moistening the skin. Apply a smaller metal pad about one-half the size of the first pad over the paralyzed side. These pads should be firmly bound on by rubber straps or by a bandage composed of such material as is used in the Bender Ideal or Ace Bandage. Gradually turn the current on, using not more than 300 to 500 milliamperes, for fifteen to twenty minutes. Reapply if there is any sensation of prickling, as prickling means poor contact, and poor contact means a burn.

2. Galvanism. After the application of heat, bind on the paralyzed side a well-moistened pad connected to the negative pole of the galvanic controller. This pad should be approximately 4 by 5 inches, and is best made of powdered asbestos with a canvas covering. Place over this pad a layer of moist absorbent cotton, thus affording a clean surface for every patient. If pain is persistent, the cotton may be moistened with a 2 per cent. solution of sodium salicylate. Similarly apply another pad, connected to the positive pole of the machine, over the cervical vertebrae, protecting the clothing from wetting by means of a small Turkish towel which has been wrapped around a piece of rubber sheeting. Then turn the current on very slowly (if this is done too rapidly the patient may become momentarily dizzy) until the point of tolerance is reached. This varies from 3 to 15 milliamperes (the metallic taste in the mouth soon ceases to trouble the patient). As a rule, after three minutes, due to the fact that the skin becomes a better conductor, there will be a slight increase in milliamperage. Give at least a twenty-minute treatment. Next, gradually turn off the current and remove the negative pad from the paralyzed side of the face and connect the negative pole of the galvanic machine to a testing electrode and determine the amount of current necessary to give a fairly vigorous muscular contraction. Stimulate the motor points of the facial nerve until there is a slight lag in the contraction. When this occurs, stop the treatment and apply a little talcum powder to the face and back to allay the irritation. Give the treatment every other day, unless (which rarely happens) the skin becomes too irritated.

Every third or fourth treatment replace the above electric stimulation by tests for the reaction of degeneration. As soon as there is response to the slow sinusoidal or Bristow faradic, use the indicated current under the same precautions for muscular tire as above. When this stage has been reached, add gentle massage for its circulatory effect, and encourage the patient to indulge in re-educational exercises. There is no means of restoring muscular tone which is comparable with the voluntary muscle impulse. These exercises should be done by the patient

before a mirror, and should be of such a character that all the paralyzed muscles are exercised. Wherever possible, bilateral action is of advantage.

#### STIFF AND PAINFUL SHOULDERS

Under this heading are included:

1. Bursitis, of which the subdeltoid variety is the most frequent.
2. Arthritis—generally of the hypertrophic type.
3. Muscle tear or stretch—especially of the spinati group.
4. Adhesions. Though these are generally secondary to a bursitis or arthritis, yet they not infrequently occur after such trauma as dislocation of the shoulder, fracture of the clavicle or elbow, etc.

The treatment depends on the existing pathology. Bursitis and adhesions due to trauma are, as a rule, more amenable to treatment than arthritis or muscle tear. In all cases a radiograph should be taken before any but the simplest remedial measures are employed. A calcified bursa might mean such a mechanical impedance to motion that operation only would accomplish functional restoration. In all cases, even including those of apparent traumatic origin, focal infection must be sought for and eradicated if present. The diet, elimination, amount of exercise, and the nervous condition of the patient should also be carefully considered and appropriate treatment ordered. For in these conditions as well as in all others physiotherapy should be an adjunct, of prime importance it is true, but nevertheless an adjunct to careful medical or surgical treatment.

At the Boston City Hospital many cases of stiff and painful shoulders are seen daily. They come in with all sorts of diagnoses—from rheumatism to neuritis—the latter diagnosis has some basis, for the pain is referred along certain nerve trunk or trunks; there is at times more atrophy than would be expected from disuse alone; there may be present some vaso-motor changes; and there are generally paresthesias, such as numbness, tingling, etc. Rarely, however, is the nerve substance really inflamed. These sensations are, as a rule, due to

mechanical pressure, and therefore it has seemed best to call such a mechanical neuritis.

The following is a typical case of group one: Miss R, aged thirty-five, comes in saying that she has pain in her right arm and shoulder. The latter is stiff and on attempted use the pain is worse. She is unable to do up her hair unless she bends her head way over to the right, while for hooking her skirt—"well it can't be done" unless she hooks it in front and then pulls it around to its proper position. She states that she fell, striking her shoulder a short time ago. Pain is worse over the area of the deltoid insertion of the humerus. At times pain will be referred along the course of the ulnar nerve. She sleeps intermittently, as pain will awaken her several times during the night. She has consulted two physicians and has been told that she had neuritis by one and rheumatism by the other. Physical examination shows none of the typical signs of a true neuritis. The radiograph is negative, thus excluding arthritis of the hypertrophic or atrophic types, and calcification of the bursa. She can raise her arm to the angle of 45 degrees, though there is pain in the attempt. On forcible manipulation it is found that the scapula moves coincidentally with the arm when a greater arc of motion than 45 degrees is attempted. The treatment in this case was:

1. Heat. External and internal baking.
2. Chlorin ionization, for its resolvent (?) effect.
3. Massage, for its circulatory effect and also to secure muscular relaxation.
4. Stretching, to break up adhesions, to increase the arc of motion, and, by lessening the pressure, to relieve pain.
5. The blue pencil static brush discharge or monopolar high-frequency vacuum tube to minimize the reaction after breaking up of adhesions.
6. Exercises.

While at first glance this seems rather a dreary and tedious treatment, yet in practice the reverse is true. The exact technic is as follows:

1. Heat. Some form of heat is indicated to relax muscula-

ture, to produce active hyperemia (thus assisting absorption), to render the skin a better conducting medium for the ionization, and to relieve pain. Some form of radiant heat, such as the electric-light baker or the so-called deep therapy incandescent light, is often all that is necessary. The length of application depends on the reaction, that is, pronounced reddening of the skin. This generally takes from ten to twenty-five minutes. If the pain is severe, diathermy (internal baking) is of value. By diathermy the deeper strictures at any desired depth may be efficiently treated. The diathermic technic is:

(1) Moisten the skin with warm soapsuds (this is not always necessary).

(2) Bind on anteriorly and posteriorly two metal disks (often-times made of 24-gage block-tin) the size of a silver dollar. Pass through the shoulder 400 to 600 milliamperes of the D'Arsonval type of the high-frequency current for at least twenty minutes. An elastic bandage is best used to secure close approximation to the skin of the metal electrodes. Be sure that no pricking ensues and that there is no faradic sensation to the current.

2. Ionization. Experience has shown that there is real value in the softening effect of the Cl. ion on adhesions and scar tissue. A 2 per cent. solution of sodium or ammonium chlorid is placed on the negative pad of the galvanic current. These pads should be fixed as in diathermy. Use 10 to 20 milliamperes for twenty to thirty minutes.

3 and 4. Massage and stretching. A *short* massage of proper character will often secure marked muscular relaxation. Then stretching should be undertaken (often when adhesions are present there will be audible snapping). The amount of stretching depends on the patient's ability to stand the pain, the readiness with which the adhesions (if present) are broken, and the ensuing reaction. In some cases the reaction is so great and so much time is lost before the next treatment (with consequent reformation of adhesions) that operation is the only rational procedure.

5. In the majority of cases though the ensuing reaction is

controlled by the use of the blue pencil brush discharge from the static or the monopolar vacuum tube (so-called violet ray) from the Tesla high frequency. These treatments, if used, should be of at least fifteen minutes' duration.

6. Between times the patient should be encouraged to exercise the shoulder. Creeping up the wall with the fingers of the disabled arm is valuable, and the added incentive of competition, that is, attempting to beat each day the height of the day before, hastens in many cases the ultimate recovery.

In some cases there is slight nerve involvement, as evidenced by paresthesias such as tingling in the fingers or such fingers as are supplied by the ulnar nerve. In such cases the slow sinusoidal water-bath is valuable. The hand is plunged in a basin of water, to which is connected one cord from the sinusoidal machine. The other cord is attached to a pad 4 x 5 inches, which is placed over the cervical vertebræ, and a current of sufficient intensity to cause gentle visible muscular contractions is allowed to flow for ten to fifteen minutes.

Recently a number of cases with calcified bursae have shown complete disappearance of the lime salts after a varying number of treatments. Whether such absorption takes place spontaneously in such cases, or whether the treatment is a contributing factor, it is impossible to state at present. At any rate, it is advisable to try this technic before resorting to surgical measures.

#### **DELAYED OR NON-UNION OF BONE**

In such conditions diathermy may be of value provided proper fixation can be secured. The rationale is simple, namely, the use of heat as a cell proliferator. Diathermy, unlike all other thermic applications, has the property of producing heat *within* the tissues with its maximum degree at almost any pre-determined depth. The bone offers more resistance, and this resistance is translated into heat, hence the bone not only becomes much hotter than the surrounding tissues, but it apparently retains this heat over a considerable period of time. The cases treated have varied in the duration of the non-union from seven weeks to twenty-seven months. Fully 80 per cent.

(where fixation is possible) have shown clinically and by the x-ray callous formation and ultimately bony union. Where fixation is impossible, the failures have equalled 100 per cent.

Two methods have been employed—the through-and-through or lateral method, and the circular or cuff method. The latter requires a longer diathermic application, but is apparently nearly as effective as the former. In cases where a plaster cast is employed, windows should be cut anteriorly and posteriorly, one a little above the fracture, the other a little below. Through these windows an appropriate strip of 22-gage block-tin should be firmly applied to the skin and a diathermic current of the D'Arsonval type of high frequency should be allowed to flow for twenty-five to forty minutes. Not over 500 to 600 milliamperes should be used. Every other day is often enough for treatment. After the fifth treatment radiographs should be taken to determine the result. Generally after the tenth treatment distinct callous formation will be present. Until there is distinct evidence of callous formation it is inadvisable to remove the fixation apparatus.

Where it is impossible to use the lateral method or there might be an element of danger due to type of fixation employed, or what not, the circular or cuff method should be used. Its technic is as follows: Cut from a sheet of 22-gage block-tin two bands long enough to encircle the parts where they are to be applied. Carefully smooth the edges of the metal so that no uneven or jagged pieces of metal can possibly abrade the skin or exert a more pronounced pressure on minute portions of the skin (if this happens the current may be more concentrated at these points and a burn may ensue). Moisten the skin with soapsuds and apply the metal bands snugly around the sites of election by means of an elastic bandage. Affix the cords from the high frequency to the metal bands and turn on 500 to 600 milliamperes of current. If there is any prickling, press the metal at that point firmly against the skin. Often the prickling is due to poor contact and this will remedy the difficulty. If the prickling still persists, readjust the metal band. Treatment should be continued until the skin between the bands becomes

thoroughly heated. This may take twenty minutes, or at times sixty, dependent on the distance between the bands, and the type of high-frequency apparatus employed. The same frequency of application and check-ups should be resorted to as in the lateral method.

In some cases one circular band may be applied around the hand and the other above the elbow. Similarly, one may be wrapped above the knee and the other encircle the instep. There is, however, a little more risk of a burn over the instep, as too much pressure may be produced over a bony prominence, and from the resulting ischemia, the circulating blood may not carry off fast enough the excess of heat. In hip fractures the anteroposterior application is the method of choice.

In all cases of non-union it is presupposed that the Wassermann reaction has been taken, and that attention has been paid to the patient's general physical condition.

#### HYPERTROPHIC ARTHRITIS

In this condition relief from pain and stiffness may be expected even though the *x*-ray findings remain unchanged. Chronic hypertrophic arthritis especially if the spurs are not in such an anatomic position as to cause nerve pressure, seems to respond as far as symptomatic relief is concerned to diathermy and medical ionization.

In stiff and painful knees, with a slight degree of roughening, the above treatment will give relief from symptoms for periods varying from six to ten months. Ordinarily repetitions of such treatments will continue the amelioration. Frequently in hypertrophic arthritis of the hip treatment confined solely to that region will also relieve referred pains to the knee. One well-marked case of hypertrophic arthritis of both hips in which pain and stiffness were present to such a degree that all exercise was out of the question, responded so well to the above treatment that he is now playing tennis three or four nights a week without discomfort. He also is able to sleep without being troubled with pain at night. Yet the marked *x*-ray pathology shows no change in character. It seems probable, therefore,

that this improvement is due to circulatory changes and lessened muscular spasm.

**Technic.**—1. Diathermy. The effects are probably thermic, resulting in a deep-seated active hyperemia, increased absorption and drainage, and relaxation of muscle spasm. The dosage depends upon the reaction, too great a milliamperage will be followed by pain. The frequency of application depends upon the degree of pain. In general it is necessary to give three treatments a week for the first two or three weeks, decreasing to twice a week, and then to once a week coincident with improvement.

*Knee-joint.*—Here the lateral application is the best. Electrodes the size of a silver dollar should be applied laterally. Every effort should be made to avoid "skin effects" by affixing them as near the exact center of the joint as is possible. Current strength, 300 to 700 milliamperes for twenty to thirty minutes.

*Hip-joint.*—The patient should preferably be recumbent. Two electrodes 5 by 3 inches with rounded ends should be placed anteriorly and posteriorly. The center of the anterior electrode should be situated over Poupart's ligament, and the posterior one directly opposite it, 600 to 900 milliamperes for twenty-five to thirty minutes.

*Wrist-joint.*—The lateral method is the best. The electrodes should be cut to such a size that there is a skin margin of  $\frac{1}{2}$  inch on either side, 200 to 400 milliamperes for twenty minutes.

*Shoulder-joint.*—The technic is described under Stiff and Painful Shoulders.

*Elbow-joint.*—The circular or cuff method is more practical here. Metal bands 2 inches in width should encircle the arm 2 inches below and 2 inches above the elbow, 300 to 500 milliamperes until the elbow feels hot to the touch.

If bilateral treatments are indicated, by the use of bifurcated cords, two similar joints may be treated at the same time. If this is done the current strength may be increased approximately 25 per cent. unless the patient complains that it feels too warm.

2. Medical ionization. Just as there is commercial electro-

plating, so in medical ionization it is possible to introduce medicinal solutions into the tissues by means of the galvanic current. This method has been overexploited. It is, however, possible to produce by ionization results which cannot be obtained by the galvanic current alone.

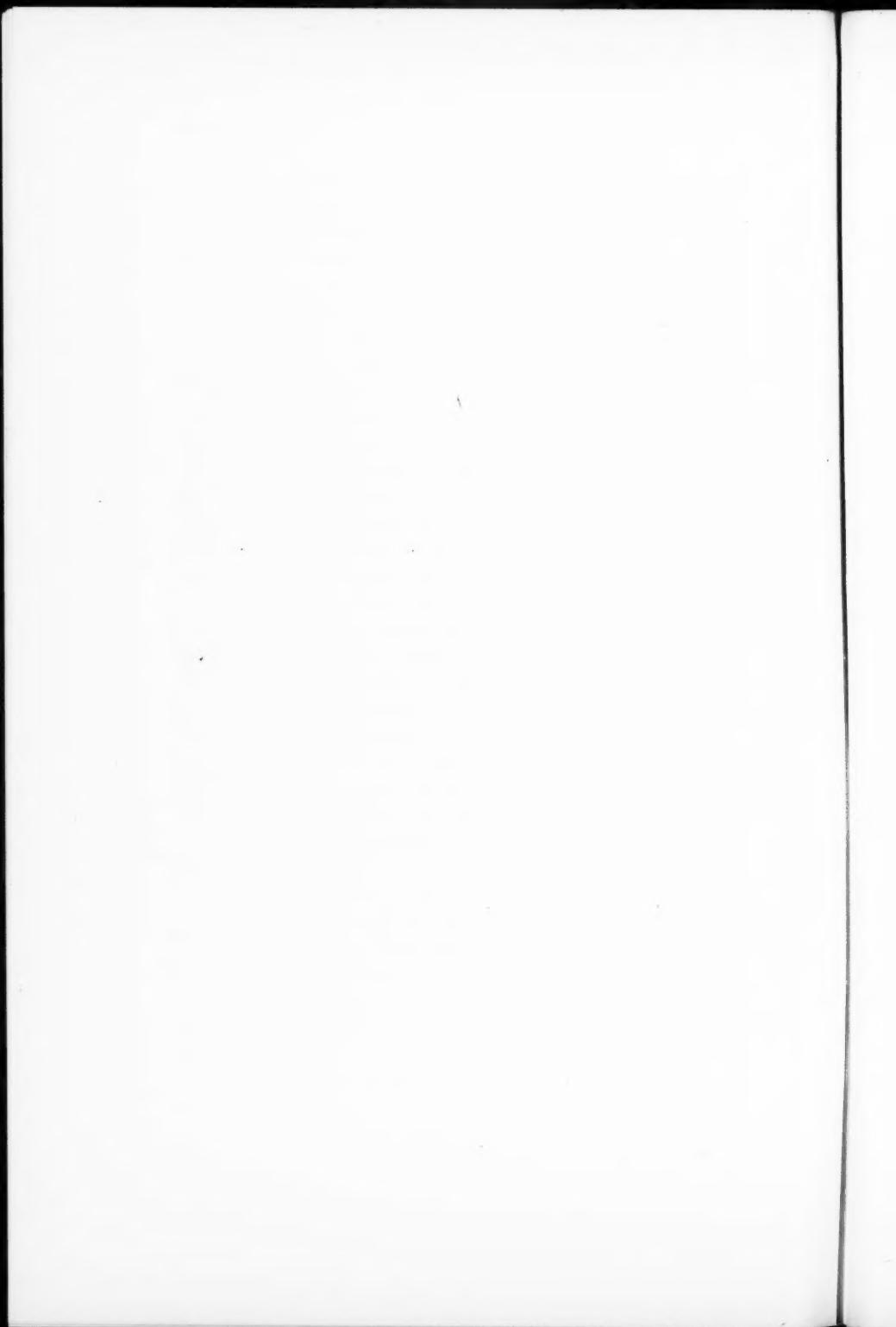
In hypertrophic arthritis three solutions may be of value:

1. Sodium salicylate on the negative pole.
2. Sodium chlorid on the negative pole.
3. Radium emanations (radium water of at least 10,000 Mache units) on the positive pole.

All these solutions except the third should not be over 2 per cent., as with this dilution there is greater dissociation and consequently more free electrons to be driven into the tissues. The pads should be of the asbestos type and should be covered with a layer of absorbent cotton which has been thoroughly wet with the desired solution. They should be applied as in diathermy, except that in the elbow-joint the anteroposterior method is the best. As much milliamperage, ranging from 3 to 30 milliamperes, should be turned on as the patient can stand without conscious effort for a period of fifteen to thirty minutes. If the skin becomes irritated, galvanism should be omitted for one or two treatments. This treatment should be applied after diathermy. Six treatments should show lessening of the pain and stiffness. Occasionally cases are made worse by galvanism. If the pain is increased after the third treatment, galvanism should be omitted and diathermy alone used.

At times the so-called "violet ray" (that is, a vacuum tube excited by the Teslar current of the high frequency) rubbed vigorously over the affected joint will relieve pain.

While from an x-ray standpoint no changes are demonstrable in hypertrophic arthritis, yet from a symptomatic one relief is marked and relatively permanent.



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**THAT DIAGNOSIS "MYOCARDITIS"**

"WHEN in doubt call it myocarditis." Such would seem to be the reasoning used in many instances in which this diagnosis is made. The dictionary defines myocarditis as an inflammation of the myocardium, but in clinical medicine the term is commonly used to include any change in the heart muscle, be it inflammatory, degenerative, or of unknown origin.

In the days preceding differentiation of the cardiac arrhythmias—*i. e.*, before the contributions to cardiology made by the polygraph and the electrocardiograph—it was common to diagnose myocarditis on the basis of an irregularity of the heart rhythm and evidence of enlargement of the organ, in the absence of murmurs pointing to valvular change. Today few would hold this conception tenable. The writer is unacquainted with any reliable criteria upon which to base myocarditis as a complete clinical diagnosis.

In the present state of our knowledge it rarely happens that it is possible to make a diagnosis of "myocarditis," or better, myocardial impairment, without there being present sufficient data on which to diagnose the underlying cause or type of heart affection, as rheumatic, syphilitic, arteriosclerotic, hypertensive, etc. The physician is not using the available information concerning heart disease nor is the patient as likely to receive the assistance to which he is entitled if the diagnosis is too lightly allowed to rest at "myocarditis." If, at the first examination, it does not seem possible to diagnose beyond "myocarditis," then there should be added, preferably in writing, "of undetermined origin." Such action will cause a sense of incompleteness and stimulate further study, as a result of which the more accurate diagnosis will often be achieved.

Acute or chronic myocarditis often appear as part of the diagnosis made by the pathologist. Let us consider briefly the changes in the myocardium that may occur in some of the more common forms of heart disease.

In rheumatic heart disease the Aschoff bodies may be found in many, but not all of the cases. These are submiliary nodules which, under the microscope, are seen to be focal collections of concentrically arranged cells in the neighborhood of minute vessels, or surrounding them. The cells are a little smaller, but otherwise much like those found in Hodgkin's disease. In the process of healing the Aschoff bodies are replaced by scars which tend to produce the picture known as "chronic fibrous myocarditis."

Septic heart disease, known by other names, such as malignant, ulcerative, infectious, or bacterial endocarditis, etc., is certainly a first cousin to rheumatic heart disease. The myocardial changes are similar to the latter, but more severe in type, and the submiliary bodies described by Aschoff are not found. There is a greater infiltration with the polymorphonuclear leukocytes and sometimes an abscess formation in the myocardium. In contradistinction to rheumatic heart disease, bacteria can often be identified in the myocardium in septic heart disease.

The changes in the myocardium in cardiovascular syphilis have been emphasized by A. S. Warthin, of Ann Arbor, and by Harlow Brooks, of New York. To quote Warthin's description,<sup>1</sup> the essential lesion is an interstitial myocarditis, characterized by infiltration with lymphocytes and plasma cells along the vessels between the muscle-fibers. The entire heart wall, from epicardium to endocardium, including the papillary muscles, may be involved in the infiltrations; but in the average case they lie nearer to the endocardium. In the great majority there are areas of healing by fibrosis associated with areas in which the process is active. The spirochetes may be demonstrated, by diligent search, in the more active areas. A progressive fibrosis of the heart muscle eventually takes place in all cases.

<sup>1</sup>Amer. Jour. Syphilis, 2, 425, July, 1918.

Sclerosis of the larger branches of the coronary arteries is rare; in the most severe cases there is infiltration around the smaller arteries. An aneurysm of the wall of the left ventricle is not uncommon. True gummata in the myocardium are relatively rare.

In arteriosclerosis the heart tends to be small, and the myocardium thinner than usual. The heart muscle is often of a brownish hue, the so-called "brown atrophy," and feels flabby to the fingers. On histologic examination, the brown atrophy is shown to be due to granules of brown pigment. Fragmentation of the muscle-fibers is common. In some cases, in which hypertension is associated with arteriosclerotic heart disease, the myocardium shows a mixed picture, *i. e.*, there is some hypertrophy of the muscle-fibers and replacement by fibrosis.

The myocardial changes in hypertensive heart disease are radically different from those found in arteriosclerosis of the senile, decrescent, or involutionary type. The myocardium is first hypertrophied rather than degenerated. It is thicker, and on microscopic examination its fibers are seen to be increased in number and size. At a later stage, when cardiac insufficiency appears, the heart muscle shows some necrosis of its fibers, with replacement by fibrous tissue, a form of fibrous myocarditis.

In the heart in hyperthyroidism the pathology is not well understood. The gross postmortem appearances are dilatation of the right chambers, and moderate hypertrophy of the left ventricle with slight fatty change. E. W. Goodpasture<sup>1</sup> has reported 2 cases in which necrosis of the muscle cells was present; he attributes this to a tonic myocarditis and not to occluding vascular lesions or local infection. The same observer, however, believes the necrosis is better regarded as the result of an injurious agent—perhaps a terminal infection—other than that responsible for the underlying cardiac disease.

In diphtheria degeneration of the myocardium is one of the common postmortem findings. The simplest form is fatty degeneration, which is found in the majority of cases. This varies

<sup>1</sup> Jour. Amer. Med. Assoc., 76, 23, 1545, 1921.

in extent, at times affecting the myocardium generally, at times occurring in foci. The fatty degeneration accompanies and seems to precede the more advanced forms of degeneration which lead to complete destruction of the muscle. Fragmentation of the degenerated muscle cells is often present. Acute interstitial lesions may be found.

**Effort syndrome:** Irritable heart is not really a cardiac disease and so there can be said to be no lesions in the myocardium.

The above résumé of the pathologic alterations occurring in the myocardium in some of the more common affections of the heart reminds us of the multiplicity of the changes to which the term "myocarditis" may be applied. Prognosis and treatment, two very important matters in each case, will surely be much less clear if we are satisfied with a diagnosis of "myocarditis," acute or chronic.

The discussion of the diagnosis "myocarditis" can perhaps be more effectively continued by some case histories. To conserve space the notes will be considerably abridged.

**Case I.**—A barber, aged sixty-one years.

Entered hospital November 29, 1922.

**Past History.**—No history of chickenpox, smallpox, measles, mumps, whooping-cough, tonsillitis, rheumatism, chorea, pleurisy, malaria, scarlet fever, or typhoid fever. Had influenza in 1919, and pneumonia in December, 1920.

Vision in right eye has failed gradually; was told that it was due to high blood-pressure; has been treated at the Eye Department.

Dyspnea on exertion has been present during the past two years. Ascending a single flight of stairs causes some palpitation; no pain in chest. Has been a patient in the hospital several times in the past two years; the dyspnea is relieved after a short stay.

**Present Illness.**—Increasing shortness of breath for three days; couldn't sleep last night because of dyspnea.

Nycturia varies from none to twice per night, dysuria two

to three; micturition apparently normal. Denies venereal infection.

Alcohol none, smokes pipe occasionally.

Weight 210 pounds one year ago, 160 pounds six months ago, and 140 pounds five months ago.

*Physical Examination.*—Well developed and nourished, cyanotic, orthopneic, and in apparent distress. Eyes: pupils equal, regular, and react to light. Ophthalmoscopic examination shows: right eye, areas of old and new hemorrhage, edema of disk; left eye, disk seems clear, no hemorrhages or exudate.

Heart: Impulse seen and felt in fifth and sixth spaces well outside nipple line. Deep cardiac dulness extends 6 cm. to right and 15 cm. to left of the midsternal line; supraventricular dulness 4 cm. Action regular, no murmurs.

Visible pulsation of carotid and brachial arteries. Blood-pressure, 180 systolic and 120 diastolic.

Abdomen: normal tympany. Liver: upper border of dulness at sixth rib, edge palpable 6 cm. below costal margin in right midclavicular line, not tender. Legs: no edema.

*Diagnosis.*—Chronic myocarditis, decompensation.

*Subsequent History.*—Received several courses of digitalis, with considerable improvement each time.

Blood Wassermann reaction negative.

Urine: Except during the attack of heart failure there was no albumin and the sediment contained no pathologic elements; a few hyaline and granular casts and as much as a slight trace of albumin appeared when heart failure was present.

Blood urea nitrogen was 17.24 mg. per 100 c.c. blood on March, 21, 1923.

On March 15, 1923 the patient developed lobar pneumonia in the left lower lobe and died on the seventh day—March 22d.

Discharge diagnosis: Arteriosclerosis, chronic myocarditis, mild hypertension, chronic nephritis (vascular), lobar pneumonia.

*Discussion.*—The diagnosis after the admission note is quite unsatisfying; that on discharge is less open to objection. From the cardiac standpoint the case is clearly one of hypertensive

heart disease and heart failure of the congestive type. As this patient was sixty-one years of age doubtless there was also some arteriosclerosis of the involutionary or senile type.

A large percentage of patients affected by high blood-pressure and in whom the diagnosis of "myocarditis" is often made are more correctly classified as victims of hypertensive heart disease. It is better to come out in the open and use the latter diagnosis, which will clarify one's thought.

**Case II**—Married woman, aged twenty-eight years.

*Chief Complaint*.—Attacks of palpitation. Was told yesterday that she had a serious disease of the heart muscle.

*Present Illness*.—During the past year has been subject to attacks of forcible beating of the heart. The attacks are associated with excitement and not with physical exertion; onset and offset gradual, heart rate during the attack estimated (by motion of the hand) to be about 100. Patient is not certain whether the rhythm is regular or irregular. The duration of the attack is variable, often several hours.

There is a sensation of fulness over the precordia, but no real pain at the time of the palpitation. There is no shortness of breath on ordinary exertion; the patient recently swam one-eighth of a mile in fresh water without untoward effects.

*Past History*.—Always "nervous." At the age of four was not thought to be sufficiently robust, and was taken to Colorado for her health. The chief symptoms were frequent vomiting and being "run down." Diphtheria at nine, typhoid fever at eleven, tonsillectomy at twelve, appendectomy at fourteen, operation for relief of hemorrhoids at twenty, and extraction of two unerupted wisdom teeth at twenty-one years, respectively. Good recovery from all of the above.

Denies rheumatic fever, severe sore throat, chorea, and pneumonia. Married a year and a half; never pregnant. States she has worried much during the past twelve months. Has been highly trained in music and practices at the piano two and a half hours daily.

*Physical Examination*.—Fairly well nourished but poorly

developed (is under the care of an orthopedist for correction of a sag to the back and a lax abdominal wall).

Heart: Impulse in the fifth space, one fingerbreadth inside the midclavicular line; percussion borders within normal limits. Soft systolic murmur with the first sound at the apex and pulmonic area. Rate varies considerably with respiration; counted as 90 per minute.

*Discussion.*—Obviously not a case of true heart disease; perhaps best considered a case of functional neurosis. Some would prefer the term "irritable heart" or "cardiac neurosis."

On the previous day the patient sent for a physician, who, she asserts, limited his examination to a brief use of the stethoscope through her waist. Then, according to the patient, he announced that there was serious "myocarditis" and imposed many restrictions upon her, particularly as regards exertion.

The writer learned later that the patient was an only daughter of wealthy parents. She had been waited upon excessively, partly because, when young, her health was considered poor. At an early age she displayed nervous symptoms and had "attacks" whenever she was not given her own way. She had been granted a divorce from a previous marriage, as she had been affected by severe nervous attacks when her husband objected to her extravagance in the use of money. As is common in cases of this type, there was much more to the patient's social history, but sufficient has been given to show the lack of nervous stability.

At this point the writer wishes to emphasize that the diagnosis of heart disease should not be made in young people without the presence of quite definite evidence, certainly more than was present in the above case. The chief reliable signs of heart disease may be listed as follows:

An aortic diastolic murmur.

Distinct overdistention of the veins of the neck.

A diastolic murmur or rumble at the apex.

A thrill at the base or at the apex. The thrill must be a definite "purr"; a slight thrill or systolic vibration may be present over the normal heart.

- Definite signs of cardiac enlargement.  
An irregular rhythm which persists after exercise (the heart rate being 120 or higher).  
A pericardial rub.  
Arterial disease or a persistent blood-pressure of 160 or more in a young person.

**Case III.**—Seamstress, aged fifty-five years.

*Chief Complaint.*—Weakness and inability to walk freely during the past two years.

*Past History.*—Measles, pertussis, and mumps in childhood. Occasional tonsillitis. Rheumatism of mild type twelve years ago. Married many years, never pregnant.

*Present Illness.*—Has been losing vigor during the past two years and is now unable to work regularly. Cannot walk far or ascend stairs because her "limbs give out." For ten months her physician has prescribed the daily use of tincture of digitalis and has told her that she is suffering from myocarditis. The patient has not improved.

Has no shortness of breath on ordinary exertion; no pain in chest or arms; ankles swell considerably at times. Present weight 165 pounds, was 142 pounds a few years ago. Her voice has become very husky and lower in pitch during the past four years. Skin noted to be dry and thicker, with some scaling. No particular change in the hair is appreciated. Patient is inclined to feel chilly; for several years she has desired an extra amount of heat in the house. Prefers hot weather; may be fatigued, but perspires freely. There is a sensation of clumsiness in the handling of her tongue, which at times appears to be thickened. Considerable diminution in power of hearing; the patient describes the present state as causing her to feel "as though in a dream" and to hear sounds somewhat "as though echoing in a large drum."

*Physical Examination.*—Well developed and somewhat overweight. General puffiness of face, more marked round eyes, flush over malar bones, expression dull save momentarily when engaged in conversation. Lips thick and of a pale, slightly

cyanotic color. Tongue and mucous membrane of mouth appear thickened and moderately pale. Teeth well cared for. Neck thick; supraclavicular pads of fat present.

Heart appears normal save for occasional extrasystoles. No murmurs detected, impulse palpable in the fifth space at the left midclavicular line, rate 80 per minute.

The skin over the body feels thickened and distinctly dry, and is slightly rough and scaly in spots. The tissues of the body



Fig. 170.—Case III. An example of so-called myocarditis relieved by thyroid extract.

and of the extremities are puffy, but pit only slightly on pressure.

*Diagnosis.*—Myxedema.

Wassermann test negative. Hemoglobin 80 per cent. Urine slightly cloudy, acid, specific gravity 1011, slightest possible trace of albumin, no sugar. The sediment contains no pathologic elements. Blood-pressure, systolic 130, diastolic 70.

Basal metabolism rate reported to be minus 32.1 per cent.

*Subsequent History.*—Very satisfactory improvement from the use of thyroid extract pills of 1 grain strength. Gradual reduction of weight to 154 pounds, and disappearance of practically all symptoms—voice, hearing, fatigue, mental dulness, chilliness, etc. Her general appearance changed so markedly that after two months many of her friends failed to recognize her.

*Discussion.*—This case is a good example of too great readiness to put the blame upon the heart and to administer digitalis as the panacea of all cardiac imperfections. The history is somewhat misleading, in that its pointing so strongly to myxedema was due to the search, by suitable questioning, for symptoms of that affection, which was suspected at first sight of the patient (Fig. 170).

**Case IV.**—A clerk, aged twenty-nine years. Entered the hospital August 10, 1922.

*Chief Complaint.*—Dyspnea.

*Present Illness.*—Perfectly well until two and a half months ago, when he had a "cold" associated with cough, sneezing, and sore throat, not severe enough to cause him to go to bed. After two days he returned to work, but at the end of about one week noted marked shortness of breath when he ascended a single flight of stairs or moved about. Obtained much relief by rest at home and the use of digitalis, prescribed by his family physician. Has a mild cough with almost no sputum; the cough brings on an attack of mild precordial distress lasting for about one-half hour. Sleeps poorly.

*Past History.*—Pneumonia at five months and at five years; complete recovery. At nineteen had typhoid fever complicated by phlebitis and ulceration of the leg; the latter was healed by skin-grafts. Severe attack of rheumatic fever eight years ago, with complete recovery. Was told there was no cardiac complication and had no symptoms suggesting impairment of the circulation. Influenza one year ago; good recovery. Has had mild tonsillitis, lasting one to two days, every winter. Cardiorespiratory history negative, save for data in the present illness.

*Physical Examination.*—Fairly well developed and nourished. No cyanosis or dyspnea.

Heart: Impulse diffuse and heaving, extends to the sixth interspace and almost to the anterior axillary line. Left border of deep cardiac dulness, second to fourth interspaces, concave to left. No supracardiac dulness. At the apex there is a soft, blowing systolic murmur almost masking the first sound and

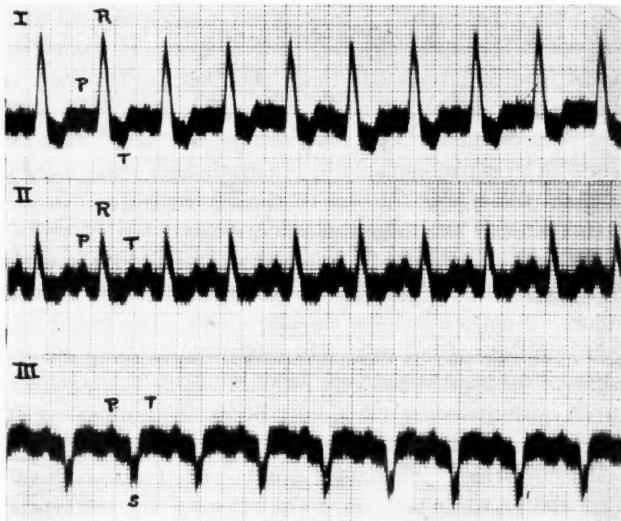


Fig. 171.—Case IV. Intraventricular heart-block, right bundle branch. Heavier abscissæ indicate periods of 0.2 second; ordinates have value of one-tenth of a millivolt.

slightly transmitted to the left. Regular rhythm, interrupted by an occasional premature beat.

The electrocardiogram (Fig. 171) shows intraventricular heart-block, right bundle branch.

*Subsequent Course.*—But slight improvement on rest in bed and the administration of digitalis. Bronchopneumonia developed about October 17th, and the patient died on October 20, 1922.

*Clinical Diagnosis.*—Chronic myocarditis, mitral regurgitation, intraventricular heart-block, bronchopneumonia, hypertrophy, and dilatation of the heart.

Autopsy: Heart: Weighs 740 gm. Very large and rather soft. The surface shows many petechial hemorrhages. On the surface of the right auricle is a radiating, thickened area of scar tissue. As the heart lies on the board it measures 20 cm. from the auricular appendages to the apex, the greatest width is 16.5 cm., the height 7.5 cm. It is especially dilated at the apex, which is round instead of conforming to the usual shape. Muscle reddish brown and thin. The chordæ tendineæ and papillary muscles are of normal appearance, showing no thickening. On sectioning the papillary muscle, however, the muscular tissue is in large part replaced by fibrous tissue. Areas of fibrosis are found throughout the wall of the left ventricle. No valve lesions are found, but the entire endocardium of the left ventricle is uniformly thickened and yellowish. At the apex is a dark red pyriform swelling, soft in the center, attached to the endocardium. Numerous smaller thrombi are found scattered about the indentations of the wall. The endocardium lining the other cavities of the heart shows very little thickening. A few strands of thickened tissue are found just below the pulmonic valve. Coronary vessels patent.

Measurements: Tricuspid valve 16 cm., pulmonary valve 8.5 cm., mitral valve 14.5 cm., aortic valve 8.5 cm., left ventricle 0.6 to 1.2 cm., right ventricle 0.5 cm.

Anatomic Diagnosis: Hypertrophy and dilatation of heart, diffuse healed endocarditis of left ventricle, fibrous myocarditis, thrombi of ventricular wall, bronchopneumonia.

*Discussion.*—The clinical diagnosis of the heart should more properly have been stated: Rheumatic heart disease, intraventricular heart-block, mitral regurgitation, chronic myocarditis.

The postmortem findings did not confirm mitral regurgitation due to lesions of the valve curtains, which is the usual understanding of this diagnosis, but from the clinical signs the inclusion of mitral regurgitation was thoroughly warranted. It

was appreciated that the symptoms were out of proportion to the findings on ordinary physical examination of the heart, and it was suspected that an electrocardiogram might disclose evidence of impairment of the myocardium. The result, a block of the right bundle branch of the conduction paths in the ventricle, justified the belief that there was considerable involvement of the myocardium. In this instance the term "myocarditis" is consistent with the rheumatic process in the heart.

The case is included in this paper because of its unusual interest and the fact, realized clinically, that myocardial damage was the essential lesion. The term "rheumatic heart disease," the writer is convinced, should have appeared on the record.

**Case V.—Married woman, thirty-eight years of age.**

*Present Illness.*—Is much overweight and is said to have "myocarditis." Has been unable to walk, except about her house, during the past ten years. At that time was ill from puerperal phlebitis and attributes her disability to the damage done her legs by the phlebitis. Has steadily increased in weight, and in the past three years has experienced shortness of breath on ascending a single flight of stairs. Present weight 340 pounds, at twenty years weighed 160 pounds, at twenty-five years, 190 pounds, at thirty years, about 190 pounds, and at thirty-three years, about 200 pounds. No pain or symptoms other than shortness of breath following exertion.

*Past History.*—Claims excellent health. At age of ten had inflammation of the bowels, not operated upon, and followed by recovery, with absence of digestive symptoms. Measles when twenty-three years of age; peritonitis of unknown origin at twenty-six years. Was ill for two months with the latter; recovery without surgical treatment.

Denies rheumatic fever, chorea, tonsillitis, scarlet fever, diphtheria, and pneumonia.

*Physical Examination.*—Obese. Heart: impulse palpable in fifth interspace at midclavicular line; no thrill. Borders of cardiac dulness within normal limits. No abnormal supra-

cardiac dulness. Soft systolic murmur with the first sound at the base and transmitted slightly toward neck. No diastolic murmur detected. Rate 70, slight respiratory arrhythmia.

Blood-pressure 175/105.

Roentgen mensuration of heart and aorta unsuccessful.

*Diagnosis.*—Obesity, normal heart.

*Discussion.*—This patient was under treatment for fibroid tumors of the uterus, and had a moderately severe secondary anemia from bleeding due to the fibroids. The anemia might well account for the systolic murmur over the base of the heart. The elevation of the blood-pressure loses some of its significance due to the abnormal amount of tissue which had to be compressed in making the test. There were no symptoms which were not easily accounted for by the obesity, manner of life, and anemia. The patient has made satisfactory improvement following treatment for the obesity, fibroids, and anemia.

**Case. VI.**—Woolsorter, aged fifty-two years. Boston Dispensary, No. 171,081.

April 21st: Is short of breath during the last three to four years. Was always strong and well previously. Has consulted several physicians; when he feels better he discontinues the use of medicine and soon relapses into feeble state.

*Physical Examination.*—Lungs negative. Heart sounds weak. Myocarditis.

Urine normal. Wassermann reaction negative.

*Diagnosis.*—Myocarditis.

July 10th: Sent to Heart Clinic. Story as above. Has cough, with about one-quarter of a cupful of sputum per day. Can ascend one flight of stairs without symptoms, but a second flight causes shortness of breath, lasting about two minutes. No pain or swelling of feet. Chief symptoms are cough, some shortness of breath, and lack of strength.

*Physical Examination.*—Chest well-marked barrel shaped; expansion much reduced. Lungs hyperresonant throughout. Breath sounds diminished, expiration prolonged; a few medium râles audible over front and back of chest.

Heart: Impulse not seen or felt. Much of cardiac area of dulness obliterated by lung resonance. Heart sounds distant. After exercise the rate is 90 per minute, rhythm regular, no murmurs detected.

Blood-pressure 115 over 90.

Sputum report: No TB. bacilli.

*Discussion.*—Faint or distant heart sounds are not sufficient evidence on which to diagnose heart disease. The readiness to resort to a loose diagnosis of "myocarditis," against which this paper is a protest, probably accounted for the failure of the previous examiner to detect the pulmonary emphysema, which was quite marked. Some degree of arteriosclerosis, consistent with the age of the patient, was no doubt present, but there was no evidence that his heart was abnormal for his years. In the experience of the writer large lung emphysema, the type present in the above case, is all too frequently overlooked in the physical examination.

**Case VII.**—Single man, aged twenty-three years. Entered Hospital March 12, 1923.

*Chief Complaint.*—Marked dyspnea of four days' duration.

*Family History.*—Negative.

*Past History.*—Recalls no previous illnesses. Denies rheumatic fever. No pain in chest. palpitation, cough, hemoptysis, night-sweats, or swelling of feet; the dyspnea was not present until recently. Best weight 140 pounds; that at present time 135 pounds.

*Present Illness.*—About four months ago first noticed shortness of breath on exertion and consulted a physician. Was told that he was not yet acclimated (came from Ireland but eight months ago). Patient was able to continue at his work; the shortness of breath has gradually increased. Not feeling quite so well the past week, but did not take to bed until yesterday. Has no pain or cough.

*Physical Examination.*—Orthopneic and cyanotic. Eyes closed, pupils react sluggishly to light and distance.

Heart: Left border of deep cardiac dulness extends to an-

terior axillary line in the fifth interspace, and to the parasternal line on the right. Impulse diffuse and soft. Soft systolic murmur with first sound at apex, and transmitted to axilla and base. Action regular, rate 90 to 100. Pulses soft and vary in volume with respiration.

Liver not palpable. No edema. Knee-jerks not obtained.

*Diagnosis.*—Dilated heart, myocarditis.

March 17th: Patient first seen by writer.

Patient rational, but disinclined to talk, apparently due to weakness.

Eyelids ptosed, but can be opened; patient can read newspaper print and does not admit photophobia.

Head falls to one side unless supported by pillows; patient has almost no control over neck muscles. Entire body is limp in a similar manner; ability to move limbs much diminished. Extremities cool, slightly cyanotic, skin moist and shows a coloration like the veining of marble (*i. e.*, cutis marmorata).

There is difficulty in swallowing and patient tries to expectorate, with indifferent success, about once a minute. The breathing simulates the Cheyne-Stokes type, but is less regular, never so deep, and the periods are shorter—three to six respirations and then a brief pause.

The cervical veins are engorged, pulsations of normal auricular type.

Liver: Upper border of dulness at the sixth rib, lower border slightly tender, two fingerbreadths below the costal border in the right mammillary line.

A moderate but definite Babinski reflex is present in the right foot; no ankle-clonus. No edema. The hands and feet look and feel like the cyanosed extremities often found in cases of effort syndrome: irritable heart when the limbs are in a dependent position.

Otherwise the physical examination was as described in the admission note.

*Discussion.*—This was obviously not the picture of severe heart failure; the ptosis of the eyelids, throat symptoms, periodic breathing, flaccidity of the body musculature, mental dulness,

vasomotor paralysis of the skin vessels, and right Babinski reflex were all foreign. A disturbance of the bulbar nuclei of the brain and perhaps some form of poisoning were suggested. The heart was, it is true, much dilated and there was evidence of circulatory failure. The diagnosis, covered by the single word "myocarditis," was, as appreciated by the service, unsatisfactory.

Further history was then sought. The patient admitted he had been in satisfactory health until March 10th; he did laboring work in a factory and was able to do reasonable lifting and carrying of boxes, etc., without symptoms. That evening he drank some moonshine and the next morning when he awoke found he was sick. The drink was stated to be as strong as the strongest whisky, and the amount was estimated equal to or a little more than 8 ounces. In the afternoon of March 11th the patient vomited and collapsed in a taxi. He was taken home and remained in bed until brought to the hospital on March 12th. The illness of four months ago, described in the history given in the admission note, was said by the patient to have been similar to the present, but less severe, and also followed indulgence in moonshine.

Death ensued at the end of March 18th. An autopsy was not obtained.

Myocarditis as the sole diagnosis has come to produce a reaction on the writer which may be expressed as "Yes, but what is it?" and this it was doubtless which caused more attention to be paid to the general symptoms, and led to further questioning, with the elicitation of the history of indulgence in moonshine. The cardiac condition may have been what French writers have termed "myocarditis éthylique"; the death, however, was primarily due to the generalized effect of some poison, perhaps wood alcohol.

#### CONCLUSIONS

There are no definite criteria upon which to base a diagnosis of myocarditis.

The diagnosis appears often to be applied in a loose way and leads to unnecessary errors.

Myocarditis is but part of a larger diagnosis, for example, rheumatic heart disease, myocarditis, etc.

In case the type of heart disease is not clear, the term "myocarditis" should be followed by the words "of undetermined origin."

Myocarditis as a primary clinical diagnosis should be abandoned; the term might well be replaced by some such expression as "myocardial impairment."

